Dissertation on

ANALYTICAL STUDY ON CLINICAL PRESENTATION AND DIAGNOSTIC IMPORTANCE IN OUTCOME OF ORBITAL MUCORMYCOSIS IN DIABETES MELLITUS

Submitted in partial fulfillment of requirements of

M.S.OPHTHALMOLOGY

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MADRAS MEDICAL COLLEGE

CHENNAI – 600 003

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI – 600003

APRIL 2016

CERTIFICATE

This is to certify that this dissertation entitled **"ANALYTICAL STUDY ON CLINICAL PRESENTATION AND DIAGNOSTIC IMPORTANCE IN OUTCOME OF ORBITAL MUCORMYCOSIS IN DIABETES MELLITUS"** is a bonafide record of the research work done by **Dr. T. LAVANNYA**, post graduate in Regional Institute of Ophthalmology, Government Ophthalmic Hospital, Madras Medical College and Research Institute, Chennai-03 in partial fulfillment of the regulations laid down by the TheTamilnadu Dr.M.G.R. Medical University for the award of M.S.Ophthalmology Branch III, under my guidance and supervision during the academic years 2013-2016.

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Finally I am indebted to all the patients for their sincere cooperation for the completion of this study.

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**ANALYTICAL STUDY ON CLINICAL PRESENTATION AND DIAGNOSTIC IMPORTANCE IN OUTCOME OF ORBITAL MUCORMYCOSIS IN DIABETES MELLITUS**" is a bonafide and genuine research work carried out by me under the guidance of my professors and assistant professors.

Date :

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CERTIFICATE OF APPROVAL

To
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Dear Dr.T.Lavannya,

The Institutional Ethics Committee has considered your request and approved your study titled **"Analytical study on clinical presentation and diagnostic importance in the outcome of orbital mucormycosis in diabetes mellitus" No.04062015.**

The following members of Ethics Committee were present in the meeting held on 09.06.2015 conducted at Madras Medical College, Chennai-3.

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2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
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We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

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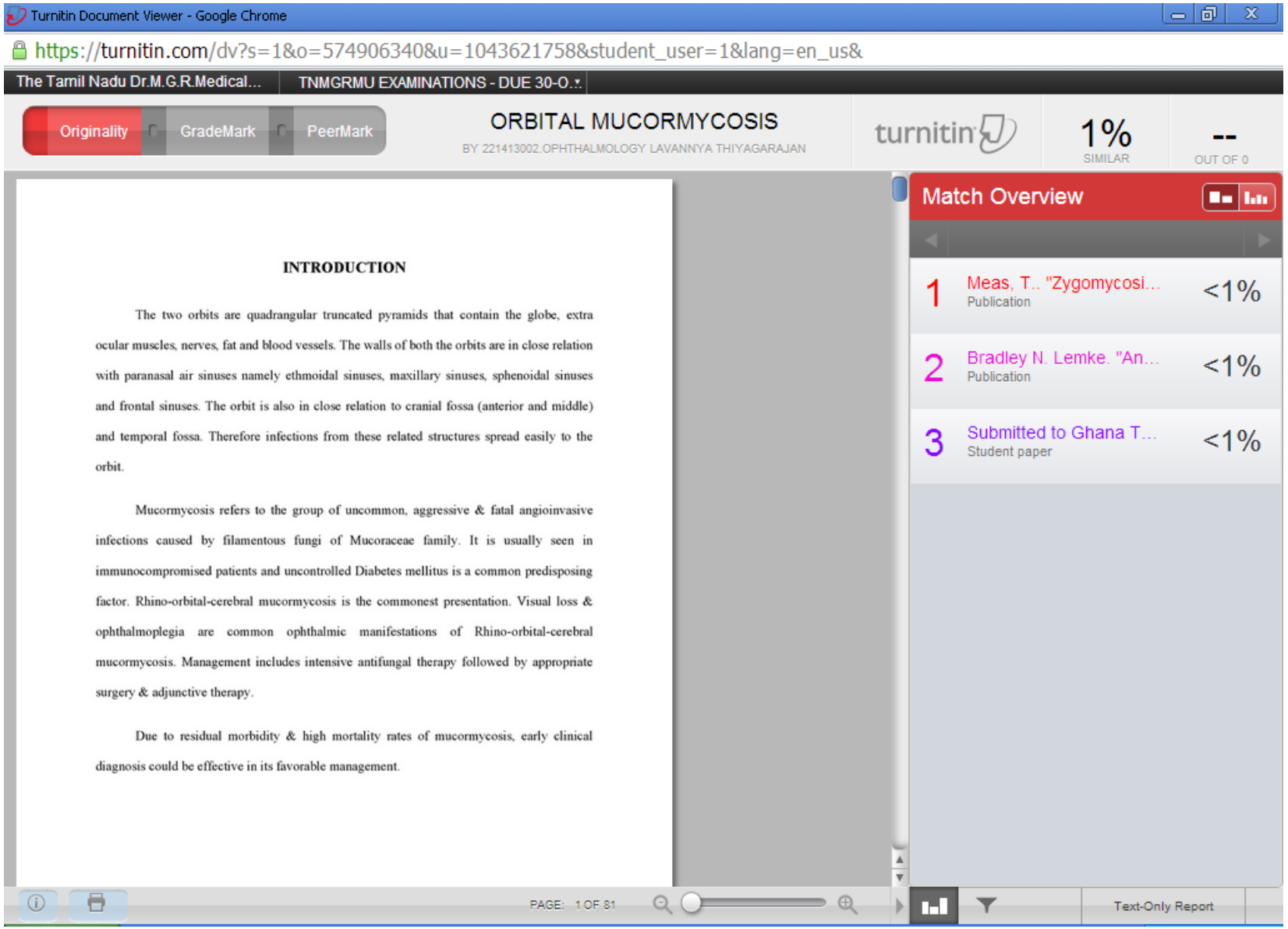
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The two orbits are quadrangular truncated pyramids that contain the globe, extra ocular muscles, nerves, fat and blood vessels. The walls of both the orbits are in close relation with paranasal air sinuses namely ethmoidal sinuses, maxillary sinuses, sphenoidal sinuses and frontal sinuses. The orbit is also in close relation to cranial fossa (anterior and middle) and temporal fossa. Therefore infections from these related structures spread easily to the orbit.
Mucormycosis refers to the group of uncommon, aggressive & fatal angioinvasive infections caused by filamentous fungi of Mucoraceae family. It is usually seen in immunocompromised patients and uncontrolled Diabetes mellitus is a common predisposing factor. Rhino-orbital-cerebral mucormycosis is the commonest presentation. Visual loss & ophthalmoplegia are common ophthalmic manifestations of Rhino-orbital-cerebral mucormycosis. Management includes intensive antifungal therapy followed by appropriate surgery & adjunctive therapy.
Due to residual morbidity & high mortality rates of mucormycosis, early clinical diagnosis could be effective in its favorable management.
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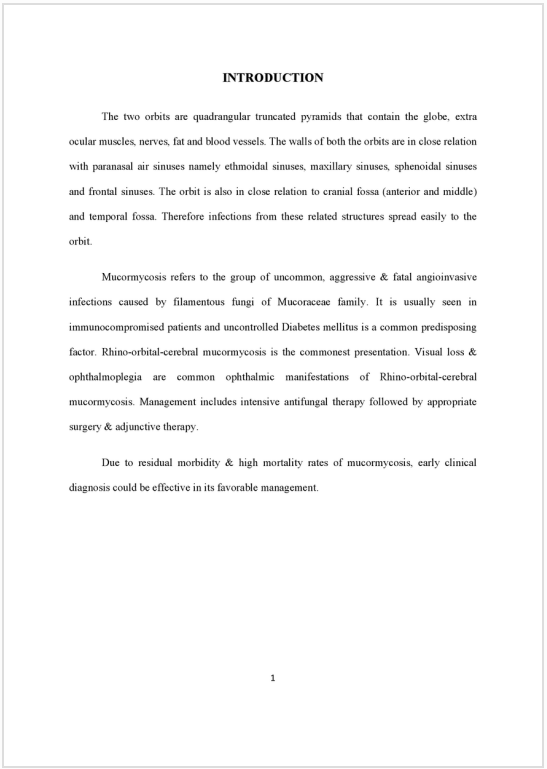

INTRODUCTION

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Due to residual morbidity & high mortality rates of mucormycosis, early clinical diagnosis could be effective in its favorable management.

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PART I

INTRODUCTION

The two orbits are quadrangular truncated pyramids that contain the globe, extra ocular muscles, nerves, fat and blood vessels. The walls of both the orbits are in close relation with paranasal air sinuses namely ethmoidal sinuses, maxillary sinuses, sphenoidal sinuses and frontal sinuses. The orbit is also in close relation to cranial fossa (anterior and middle) and temporal fossa. Therefore infections from these related structures spread easily to the orbit.

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REVIEW OF LITERATURE

Perspective study on Mucormycosis by Sellberg et al shows that mucormycosis is a life endangering fungal infection that occurs in immunocompromised patients. Even though, these infections are increasing day by day, survival rate is very poor.

Only by proper understanding of the species of fungi and the various pathogenic mechanisms involved we can find a solution to this condition. From these studies we can very well come to know that iron, is important in regulation of mucormycosis and deferoxime supplement the needed iron to the organism and enhance its growth. So therapy with iron chelator is used in treating the dreadful condition. Recent studies have shown the use of liposomal amphotericin in higher dose. Lipid based amphotericin, an echinocandin, an azole or a combination of all three can be used. The principle therapy of Rhino Orbital Cerebral Mucormycosis is early diagnosis, identifying the various risk factors and taking measures to reverse them and intervene at proper time by surgical measures.

According to Lanternier et al, in 2005-2007, there is a sex predisposition and men are affected .The affected patients are in the age group of fifty. Two weeks is the duration between the entry of organism and its manifestation. R.Oryzae is one of the most common fungal organisms.

As per George Petrikkos et al in 2012, Mucormycosis is an angioinvasive infection caused by filamentous fungi, of mucorales order belonging to zygomycetes class. The patients with poor glycemic status are more prone for this disease. Epidemiology, various symptoms and signs and cause for deterioration of vision are studied.

As per RA Yohai et al in the year 1994, analysis of factors involved in prognosis of mucormycosis was done and data collected.

- Various associated factors which predispose to mucormycosis
- Orbital and ocular symptoms and signs-incidence
- Nonocular symptoms and signs-incidence
- Time duration between symptom onset and treatment
- Imaging studies showing the involvement of various sinuses during surgery

Causes associated with decrease in survival rate

- Late diagnosis and delayed treatment
- Bilateral sinus involvement
- End stage renal disease
- Leukemia
- Desferoxamine therapy

As per AM Sugar et al in1992, mucormycosis is an air borne infection which mainly involves the paranasal sinuses which spread to orbit and then to the brain. Patients with ROCM should be aggressively treated with i/v amphotericin B and surgical debridement.

According to Ravindra V Shinde et al in 2013, orbital mucormycosis is a rare and life threatening infection that occurs in patients with diabetes mellitus. Early recognition and treatment are essential because it may lead to death in few days.

As per Moht Hayat et al in 2013, this uncommon aggressive angioinvasive fungal infection occurs in immunocompromised states like diabetes mellitus, chronic renal failure and desferrioxamine therapy. The prompt initiation of amphotericin B therapy with surgical debridement and supportive care is essential in successful management of ROCM.

ANATOMY OF THE ORBIT

EMBRYOLOGY AND DEVELOPMENT

Orbit develops around the eyeball. It is derived from the mesenchyme which encircles the optic vescicle and the optic stalk, above from the mesodermal capsule of the forebrain, below and laterally from the maxillary process, medially from fronto-nasasl process and posteriorly from pre and orbito-sphenoid. The differentiation of the bones starts by the third month and later undergoes ossification and fusion. Though the eyeball reaches adult size by three years of age, the orbit continues to grow until puberty.

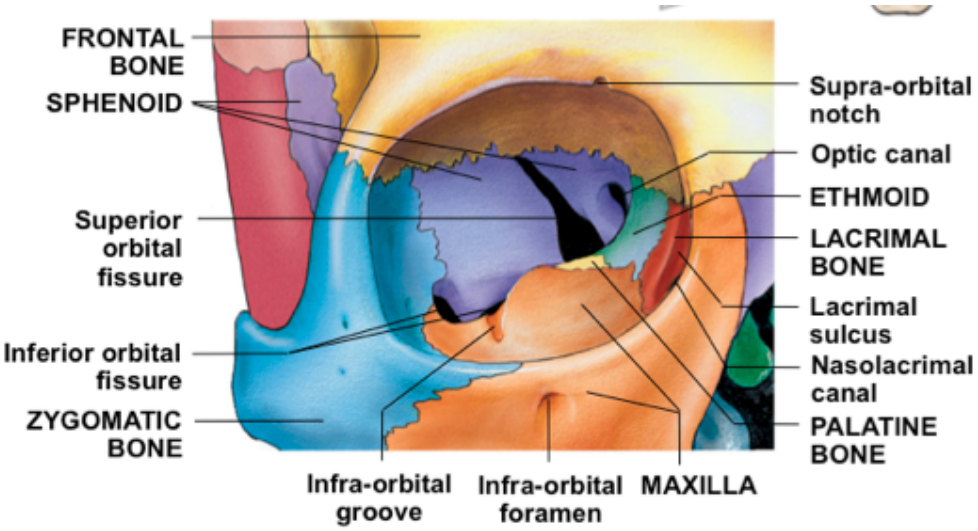
GENERAL ANATOMY:

There are seven bones which form the orbit

1. Frontal
2. Ethmoidal
3. Lacrimal
4. Palatine
5. Maxillary
6. Zygomatic
7. Sphenoid

The walls in the medial aspect of each of the orbit are aligned in such a way that they are parallel whereas the lateral walls are perpendicular. The lateral wall meets the medial wall at 45 degree angle.

THE BONY ORBIT



DIMENSIONS OF THE ORBIT:

Volume – 30 cubic cm

Height - 35 mm

Width – 40 mm

Length of the medial wall – 45 mm

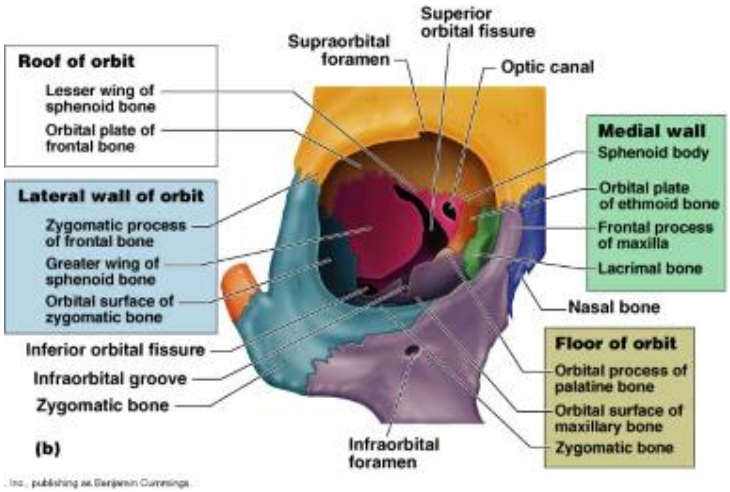
Intra orbital width – 25 mm

Distance between the two lateral orbital margins–100mm

Orbital index – height/width * 100

ORBITAL WALLS:

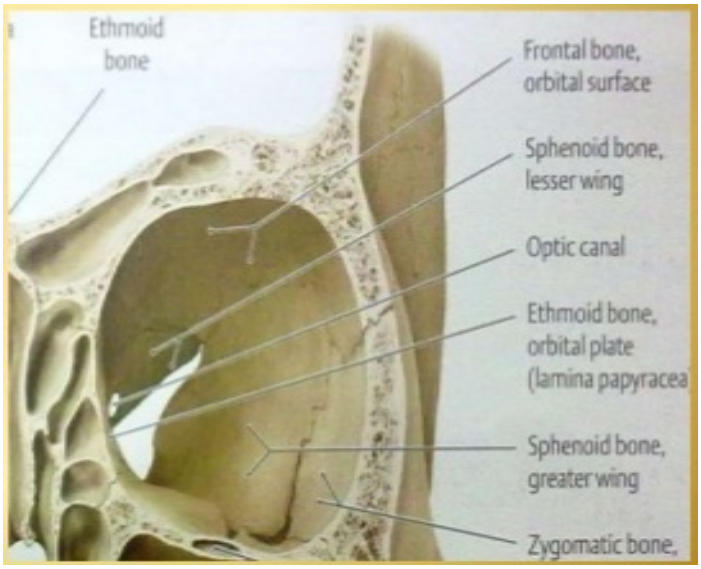
The walls which form the orbit are four in number.



1. Roof
2. Medial wall
3. Floor
4. Lateral wall

They are covered by the periosteum.

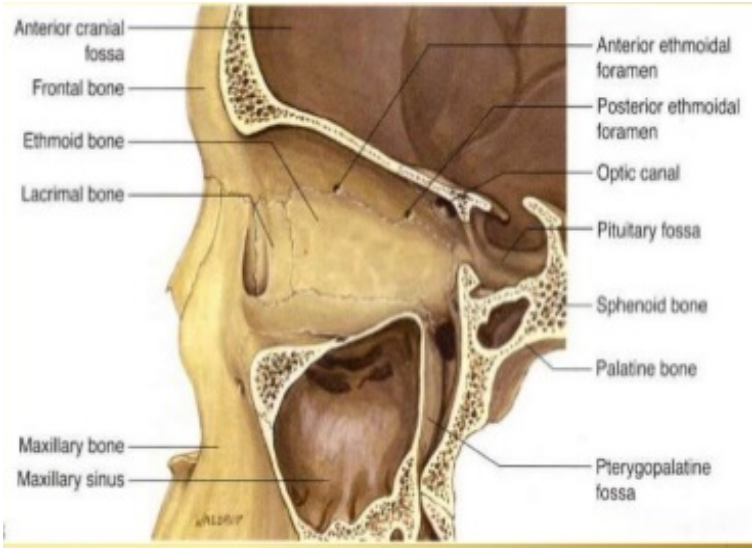
ROOF:



Orbital surface of frontal bone and sphenoid (lesser wing) make the roof or vault. It is triangular in shape. It has concavity in the anterior part and is relatively flat in the posterior part. At a distance of 1.5cm from the orbital margin, the concavity of orbital roof is more to engage the equator of eyeball.

Anterolateral part of the roof has a fossa for the lacrimal gland. The frontal sinuses are related to the anteromedial part of vault. The spine which has a pulley for the superior oblique muscle to pass through is located in a depressed area which is about 4 mm away from the medial margins of the orbit. The frontal lobe of the brain is separated from the orbital cavity by the roof. Due to old age, part of the bone which forms the roof becomes sclerosed and it can become damaged easily.

MEDIAL WALL:



The shape of the medial wall is quadrilateral.

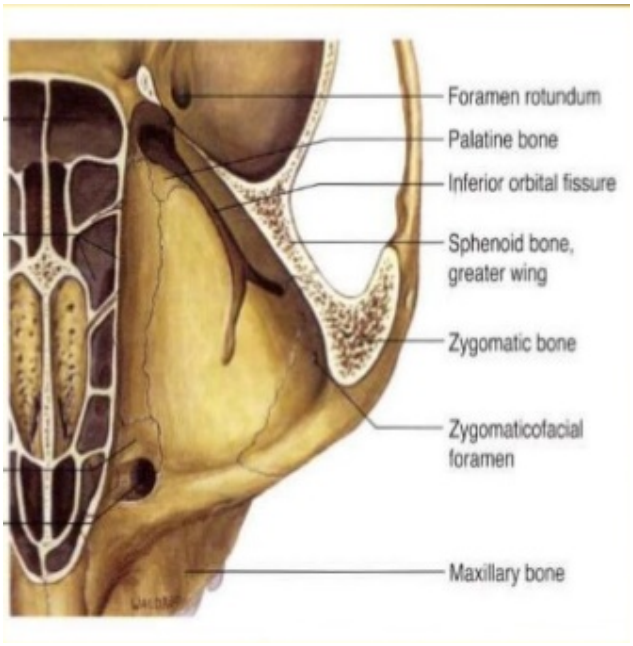
It is formed by bones namely,

1. Maxillary frontal process
2. Ethmoidal orbital plate
3. Sphenoid bone (Body of sphenoid)
4. Lacrimal bone

The thinnest orbital wall is the lamina papyracea, which is 0.2-0.4 mm thick. It's paper thin and has perforations for blood vessels and nerves. Infection from ethmoidal sinuses can rapidly spread to the orbit via this thin bone and hence bilateral orbital cellulitis is

common in younger age group. The medial wall of the orbit contains fossa for the lacrimal sac in its anterior aspect. Fossa of lacrimal sac is bound anteriorly and posterioly by lacrimal crest. Maxillary bone (frontal process) constitutes the lacrimal crest which is anterior and lacrimal bone, which forms the lacimal crest that is posterior.. Medial aspect of medial wall has anterior ethmoidal air sinuses, posterior ethmoidal air sinuses, middle meatus of the nose and sphenoidal sinuses.

FLOOR:

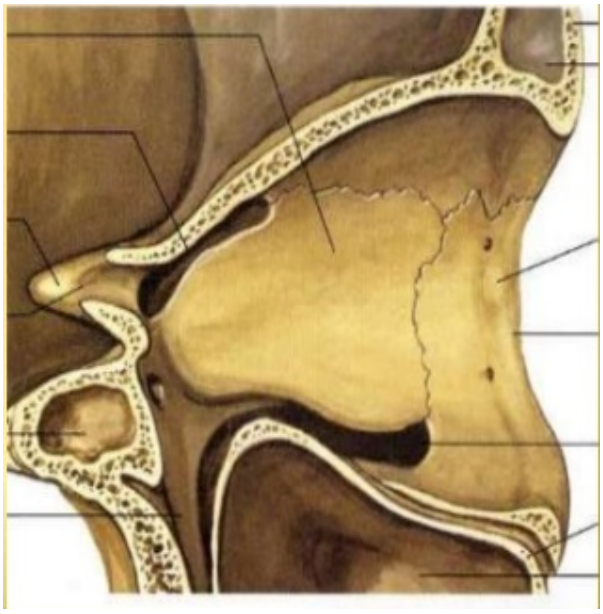


It is triangular in shape formed by,

1. The Maxillary bone
2. Palatine bone
3. Zygomatic bone

The orbital fissure (inferior) is located in posterior part of the floor of the orbit. It separates orbital floor from lateral wall. Its running forward from the fissure is the orbital groove which is located inferiorly. This groove continues as the orbital canal inferiorly which opens into the infra orbital foramen just below the inferior orbital rim. The infra orbital vein and artery run in this canal. The inferior wall is related to the maxillary air sinuses.

LATERAL WALL:



It is triangular in shape. The wall is very thick and strong.

BONY RELATIONS:

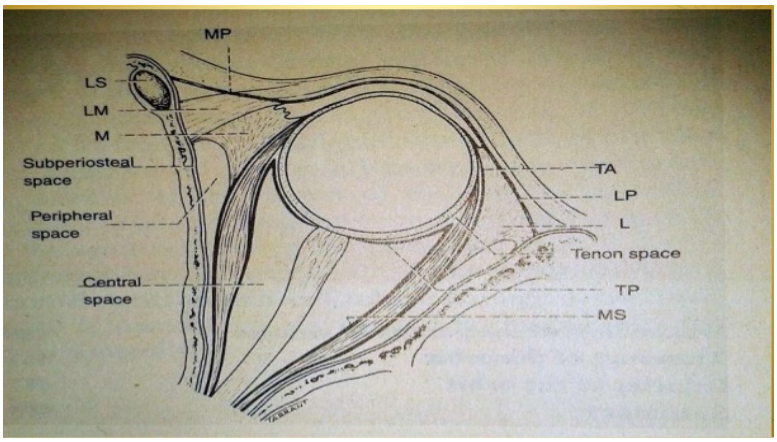
Orbital surface of the zygoma forms the anterior third.

Orbital surface of greater sphenoidal wing forms the posterior third.

It extends up to the equator of the globe anteriorly and thereby protects the posterior aspect of the eyeball and help in peripheral vision. The important landmark in the anterior

part of this wall is the anterior tubercle of Whitnall. To this is attached the suspensory ligament of the lateral rectus muscle, suspensory ligament of eyeball, temporal horn of levator aponeurosis and lateral canthal tendon.

SURGICAL SPACES OF ORBIT:



There are a number of spaces in the orbit. As per the surgical point of view, there are four main spaces in orbit.

1. Sub tenon's
2. Central
3. Peripheral
4. Sub periosteal

SUBPERIOSTEAL SPACE:

This is an important space which lies in between the orbital bones and the periorbita. Anteriorly this space is limited by its strong attachment of the periorbita to the orbital rim.

Mucocele, dermoid cyst, epidermoid cyst, myelomas, osteomas, hamartomas, fibrous dysplasias and subperiosteal abscess are common in this space.

PERIPHERAL SPACE:

This space lies between the four extra ocular muscles with their intermuscular septa which lies internally and periorbita peripherally, septum orbitale anteriorly and it is continuous with the central space posteriorly. The following structures are found in this space namely fat and muscles which include superior obique, inferior oblique and levator palpebrae superioris. The following nerves are found in this space namely lacrimal, frontal, nerve to superior oblique and ethmoidal nerve (anterior and posterior). It contains (inferior and superior) ophthalmic veins, lacrimal gland and part of lacrimal sac. Lesion arising from this space produces eccentric proptosis. The common lesions in this space are childhood capillary haemangioma, pseudotumour of the orbit, benign and malignant tumours of the lacrimal gland and the malignant lymphoma. The lesions can be explored by anterior or lateral orbitotomy

CENTRAL SPACE:

This space is also called posterior or the retro bulbar space or the muscle cone. Tenon's capsule bounds it anteriorly which lines the posterior aspect of the eye and the extra ocular recti muscles with inter muscular septa which form the periphery of this space. This space is continuous with peripheral orbital space in the posterior aspect.

Main content of this space includes,

1. Second nerve and its surrounding meninges,
2. Oculomotor nerve divisions (superior and inferior)

3. Nasociliary (branch of ophthalmic division of fifth cranial nerve)
4. Sixth cranial nerve
5. Ciliary ganglion
6. Ophthalmic vein (superior), ophthalmic artery
7. Orbital fat

Lesion in this space produces axial proptosis. The space is approached by lateral orbitotomy, the lesions being optic nerve glioma, cavernous haemangioma, orbital meningioma, neurofibroma and neurilemmoma.

SUBTENON'S:

This space is located in between sclera and tenon's capsule and is seen around the eyeball. Whenever there is infection in this space, drainage of the inflammatory material is done by making an incision in the conjunctiva and tenon's capsule.

MARGINS OF THE ORBIT:

The orbital margins are quadrilateral in shape and the corners appear to be rounded and spiral.

The superior margin is continuous with the lacrimal crest which is located posteriorly and the inferior margin with the lacrimal crest which is located anteriorly. The length of each orbital margin is 40 mm and the width is more than the height. The orbital margins are mainly formed by frontal, Zygomatic and maxillary bone.

SUPERIOR MARGIN:

The frontal arch forms the superior margin. 25 mm medial to the midpoint of the superior orbital margin is found a notch. The lateral portion of the superior orbital margin is sharp and medial portion is rounded. The supra orbital nerve and the artery traverses the supra orbital notch. Supra trochlear groove is found 10 mm medial to the notch in the superior margin. This groove transmits supra trochlear nerve and artery.

LATERAL MARGIN:

The zygoma and frontal bone's zygomatic process forms lateral margin. This margin does not reach as far anterior as the medial margin and hence the anterior part of the globe is not protected by the bone laterally.

INFERIOR MARGIN:

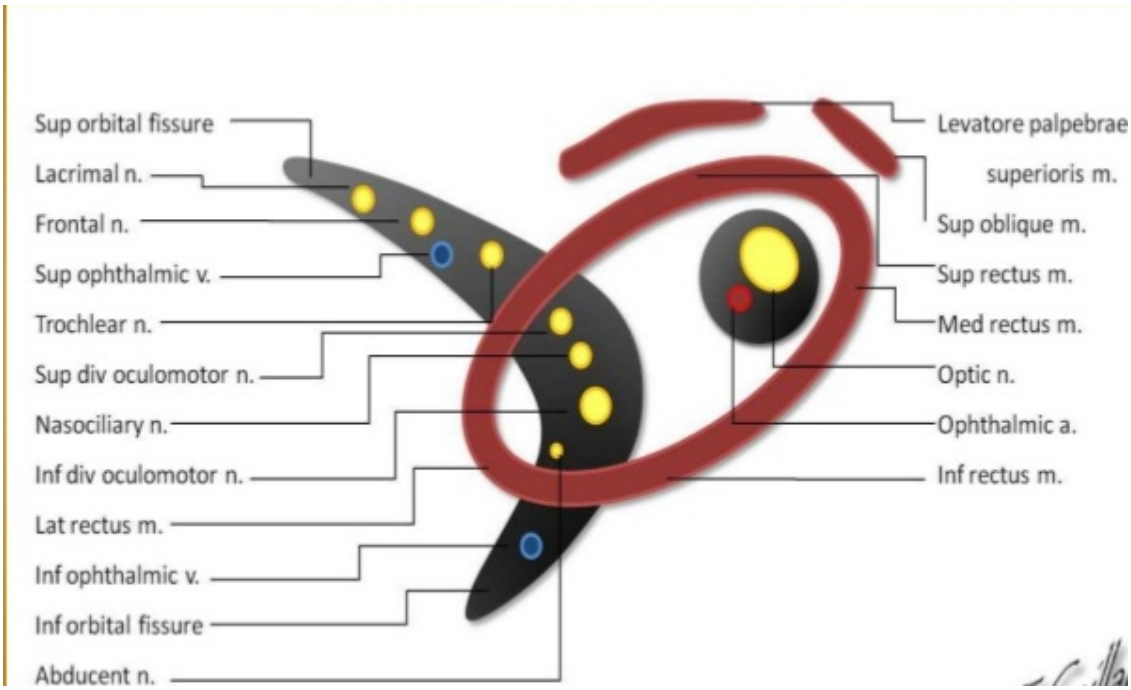
It is formed in equal proportion by the maxilla in the medial aspect and the zygomatic bone in the lateral aspect. About four mm below the orbital margin in line with the supraorbital foramen is the infra orbital foramen through which passes the infra orbital nerve and vessels. The suture between the two bones is felt about half way along the margin which forms a tubercle.

MEDIAL MARGIN:

Frontal bone above and maxilla (frontal process) below forms the medial margin. It is not continuous.

FISSURES IN THE ORBIT

SUPERIOR ORBITAL FISSURE:



It's a comma shaped aperture in the orbital cavity, also called the sphenoidal fissure. It separates two wings of sphenoid and is 22 mm in length. Orbital cavity is connected to middle cranial fossa through this fissure. The medial end is wider and it narrows laterally. The common tendinous ring spreads from medial to lateral part and divides the fissure in to three parts.

Upper part transmits,

1. Frontal nerve
2. Nerve to superior oblique muscle
3. Lacrimal nerve

4. Ophthalmic vein (superior)
5. Recurrent lacrimal artery.

Middle part transmits,

1. Divisions of third nerve(superior and inferior)
2. Abducent nerve
3. Branch of ophthalmic division of fifth nerve (Nasociliary)
4. Sympathetic roots (ciliary ganglion).

Lower part transmits,

1. Inferior ophthalmic vein
2. Sympathetic nerve plexus

INFERIOR ORBITAL FISSURE:

It is located between lower orbital margin of sphenoid (greater wing), maxilla and palatine bone (orbital process), also called as Sphenomaxillary fissure. It connects orbital cavity with pterygopalatine and infratemporal fossa.

It lies inferolateral to optic foramen. The peri orbital and Mullers muscle closes the fissure. The central part is narrow. The size of fissure depends on stages of maxillary sinus development and so younger age group have wider fissure.

Following structures traverse the fissure namely,

1. Infraorbital and zygomatic nerves
2. Nerves from sphenopalatine ganglion
3. Branches of ophthalmic vein (inferior)

OPTIC CANAL:

It is 8-10 mm long and located in the sphenoid bone (lesser wing). This canal is separated from Orbital fissure (superior) by a bony strut. This connects apex of orbit with middle cranial fossa.

The canal is oval in shape and vertically it has larger diameter. The middle part is circular and it is transverse in the cranial end. The orbital end of canal is the optic foramen, which is less than 6.5mm in vertical aspect and 4-4.5mm in horizontal aspect in adult. There is a close relation between this canal with the sphenoid and ethmoid air sinuses. Superiorly it is related to olfactory tract and gyrus rectus.

The following structures traverse the canal,

1. The optic nerve with its meningeal coverings
2. Ophthalmic artery and
3. Sympathetic plexus which surrounds the artery.

ORBITAL RELATIONS

SUPERIOR RELATIONS:

Frontal bone (orbital part) which constitutes roof separates orbit from frontal air sinuses and occasionally the ethmoidal air sinus that invades the roof. Frontal lobe of brain and their meningeal layers are superior to the roof.

The roof is close to the following structures namely supraorbital artery and frontal nerve which is close to periorbita. Levator palpebrae and superior rectus are seen below the roof. In between roof and medial wall is the superior oblique muscle.

MEDIAL RELATIONS:

The lateral nasal wall, infundibulum, ethmoidal air cells and sphenoidal air sinus form the medially related structures of the orbit. At posterior end of medial wall is the optic foramen.

The lacrimal sac with its fascia is seen here anteriorly. The orbicularis oculi muscle, septum orbitale and check ligament of medial rectus are found behind it. The ethmoidal nerves (anterior and posterior) and the infratrochlear nerve are seen in between the medial rectus and superior oblique muscle.

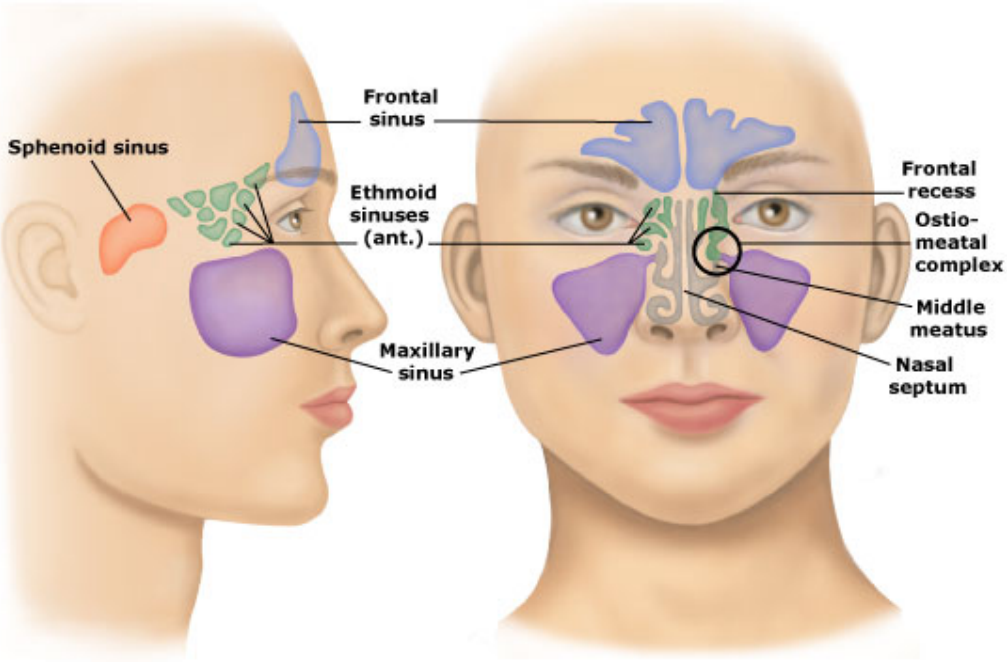
LATERAL RELATIONS:

Temporal fossa with temporalis muscle is found anterior to lateral wall and in the posterior part is the middle cranial fossa, meninges and temporal lobe.

INFERIOR RELATIONS:

Maxillary sinus is located inferior to the orbit. Infraorbital nerve and vessels are seen to course inferiorly. Inferior rectus, inferior oblique and orbital fat pad are related inferiorly to the orbit.

PARANASAL SINUSES



The Para nasal sinuses are air filled spaces in the maxilla, frontal bone, sphenoid and ethmoidal bone. These differ in shape and size in individuals according to their age. These spaces are lined by mucoperiosteum. They connect with both nasal cavities via small holes.

MAXILLARY SINUSES:

These are paired sinuses. They are the largest of the para nasal sinuses and are situated in the maxilla.

The cavity is pyramidal in shape. A part of lateral aspect nose is formed by base of the pyramid and apex of maxillary sinus extends inside zygomatic process of maxilla. The maxillary orbital plate forms the roof. It contains infra orbital vessels and nerve. The alveolar process contributes to floor of the maxillary air sinus.

The alveolar nerves and blood vessels run in canals that are located in the anterior wall. The posterior wall contains posterior superior alveolar nerves and vessels. Infra temporal fossa is found adjacent to the posterior wall. Medial wall is also called base. Maxilla predominantly forms medial wall. It is also formed by uncinate process of ethmoid, palatine bone.

The maxillary sinus has opening in middle meatus of nose through one or more openings that pierce hiatus semilumaris via superior part of medial wall.

Nerve supply:

1. Infraorbital nerve
2. Alveolar nerve – Anterior
3. Alveolar nerve - Middle
4. Alveolar nerve - Posterior
5. Alveolar nerve - Superior

Blood supply:

Arterial supply:

1. Anterior alveolar artery
2. Posterior alveolar artery

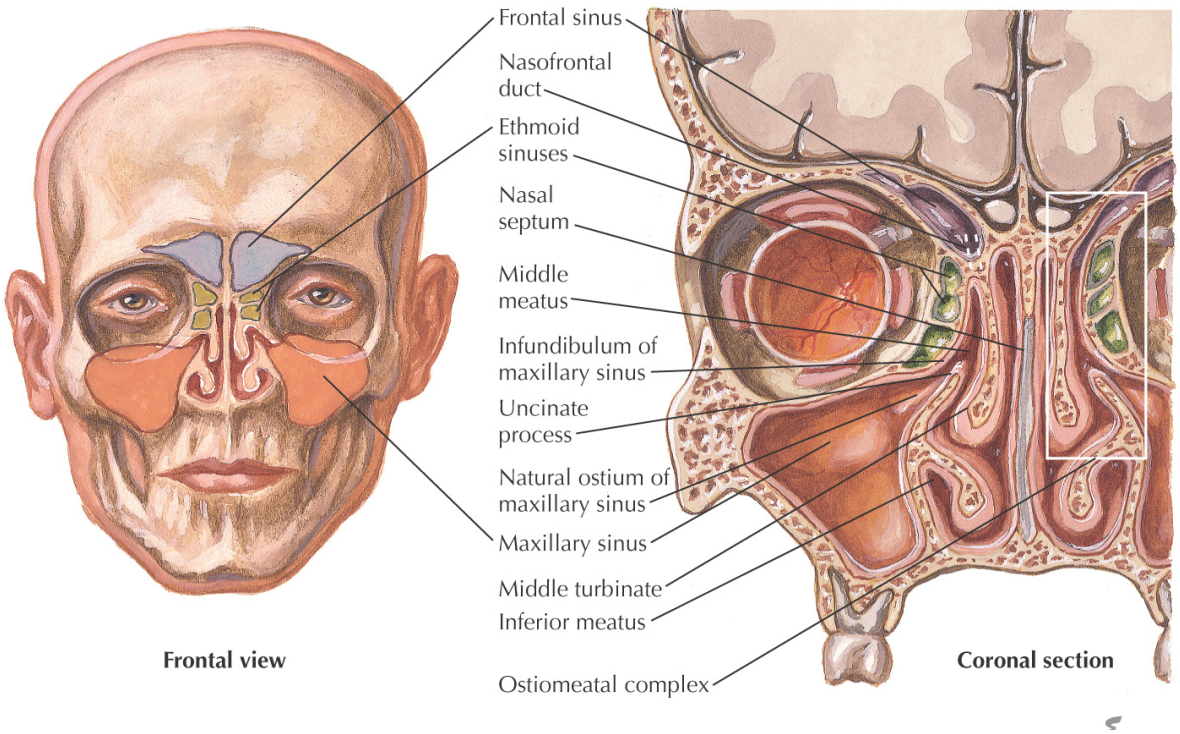
Venous drainage:

Corresponding Venous plexus of nose

Lymphatic drainage:

Nodes in sub mandibular region

FRONTAL SINUSES:



These are paired air spaces one in each frontal bone. The bony septum divides them in to two. Each sinus is divided into many small recesses by tiny partitions of bone. The shape of each sinus is a triangle. The medial end extends above the eyebrow and posterior to the medial end of roof of the orbit.

RELATIONS OF FRONTAL SINUS:

ANTERIOR:

Supra orbital nerve

Supra trochlear nerve

POSTERIOR:

Frontal lobe

Meninges

INFERIOR:

Orbit

Nose

The frontal sinus opens into middle meatus of nose through fronto nasal duct of ethmoidal infundibulum via hiatus semilunaris. Opening of frontal sinus is located close to the opening of anterior ethmoidal and maxillary sinus.

Nerve supply:

Superior orbital nerve

Blood supply:

Arterial supply:

1. Superior orbital artery
2. Ethmoidal artery(Anterior)

Venous drainage

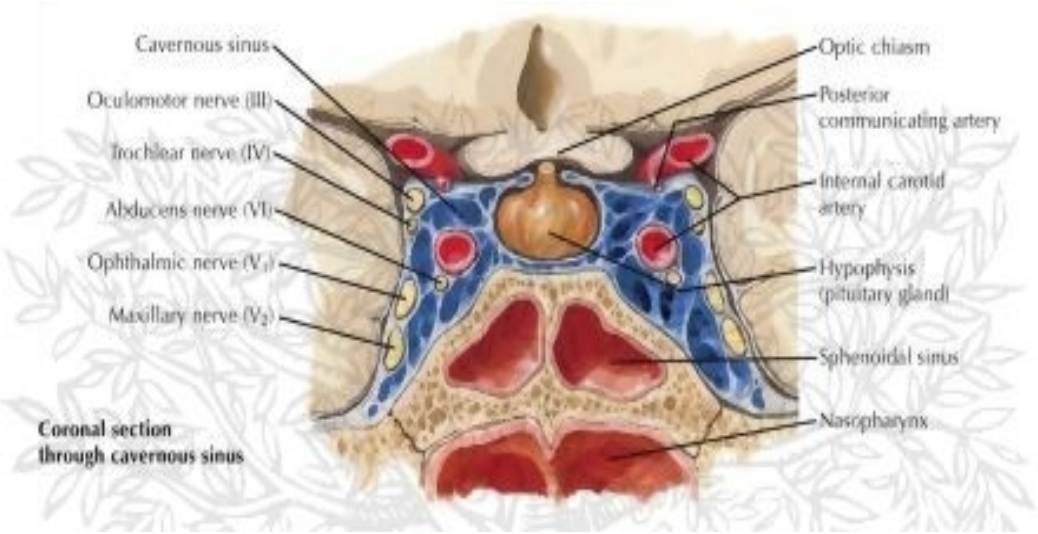
1. Venous plexus of nose
2. Superior orbital veins

Lymphatic drainage:

Sub mandibular lymph nodes.

SPHENOIDAL SINUS:

The sphenoidal air sinuses are paired air filled spaces that are seen in the body of sphenoid. Extent and development of sphenoid sinus are greatly variable. A vertical septum divides the two sphenoid sinuses. This septum which is seen in the midline is often deviated to one side.



RELATIONS OF SPHENOID SINUS

ANTERIOR:

Cavity of nose

Ethmoid sinus

POSTERIOR

Cranial fossa

Pons

LATERAL:

Cavernous sinus

Internal carotid artery

Nerve to lateral rectus

SUPERIOR:

Optic nerve

Optic chiasma

Hypophysis cerebri

INFERIOR:

Nasopharynx

Pterygoid canal.

Opening of sphenoidal sinus is in to the nose and recess of Sphenoid and ethmoid.

Nerve supply:

1. Ethmoidal nerve
2. Branches of pterygo palatine ganglion

Blood supply:

Arterial supply:

Ethmoidal arteries

Venous drainage:

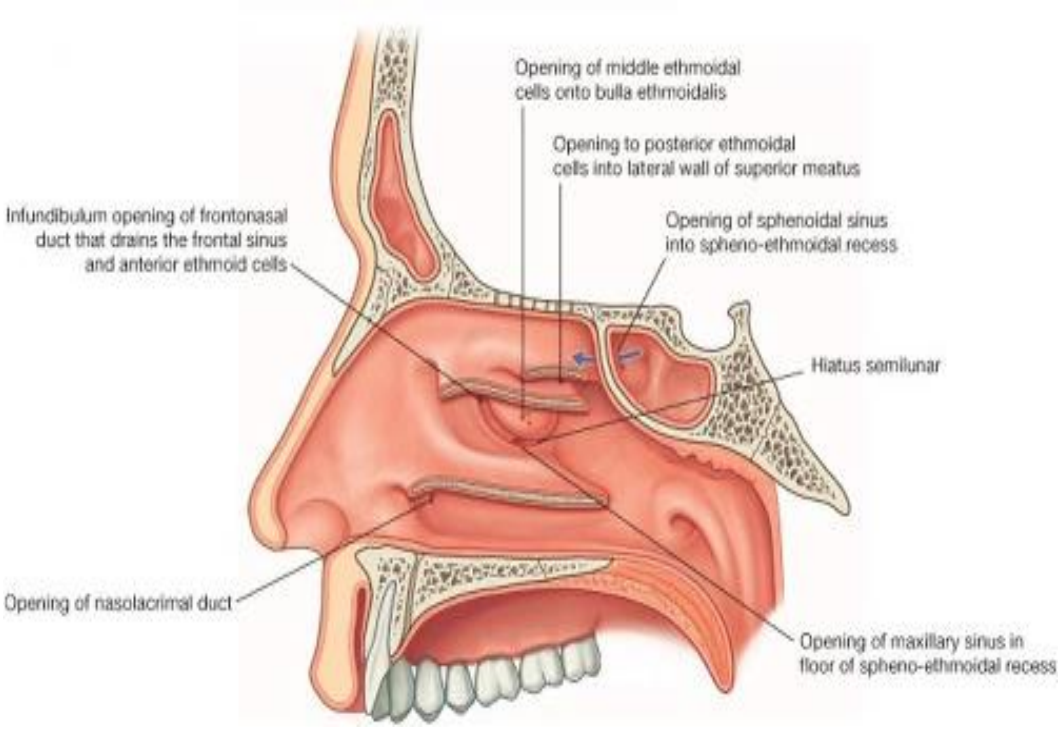
Ethmoidal veins (Posterior)

Lymphatic drainage:

Lymph nodes in retropharyngeal space

ETHMOIDAL SINUSES:

The ethmoidal sinuses are paired air filled cavities in the ethmoid bone. It has honey comb like air spaces. The number of air cells range from three to eighteen. There are three groups of ethmoidal air cells. They are called anterior, middle and posterior ethmoidal air cells.



RELATIONS OF ETHMOID SINUS:

SUPERIOR:

Frontal lobe

Anterior fossa

Meninges

INFERIOR:

Nasal cavity

MEDIAL:

Nasal cavity

LATERAL:

Cavity of nose

Infections causing orbital cellulitis frequently and more easily spread from ethmoid sinuses into the orbit. This is because the wall that separates the two structures is very thin.

Anterior and middle group of air cells open inside middle meatus of the lateral wall of nasal cavity. Anterior cells open by minute openings through infundibulum of ethmoidal bone or fronto nasal duct. Clusters of air cells present medially open via bulla ethmoidalis. Posterior air cells open into superior meatus.

Nerve supply:

1. Ethmoidal nerves (anterior and posterior)
2. Branches from pterygo palatine ganglion

Blood supply:

Arterial supply:

Ethmoidal artery (anterior and posterior)

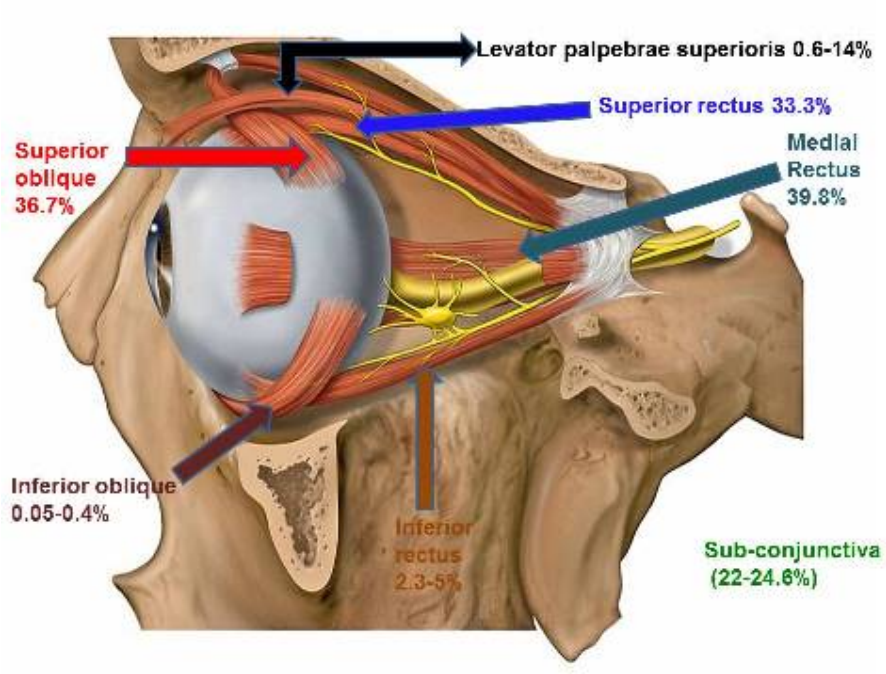
Venous drainage:

1. Anterior ethmoidal veins
2. Posterior ethmoidal veins

Lymphatic drainage:

1. Nodes in Submandibular region
2. Retropharyngeal nodes

CONTENTS OF THE ORBIT



The total volume of orbit is 30cc. The following structures contribute to it,

1. THE EYEBALL

2. ORBITAL FASCIA

    a. Fascia bulbi

    b. Fascial sheath of the muscle

    c. Check ligaments

    d. Connective tissue supporting the orbital fat

    e. Periorbital membrane

    f. Orbital septum

3. MUSCLES

    Extra ocular muscles

        a. Recti-Lateral,Medial, Superior, Inferior

        b. Oblique-Superior and inferior

        c. Levator palpaprae superioris

    Smooth muscle

        Mullers muscle

4. ARTERIES

    a. Ophthalmic artery

    b. Infraorbital artery

    c. Branches of Middle meningeal artery

5. VEINS:

    a. Superior ophthalmic vein

    b. Inferior ophthalmic vein

    c. Central retinal vein

6. NERVES:

        a. Second cranial nerve- Optic nerve

        b. Third cranial nerve- Oculomotor nerve

        c. Fourth cranial nerve- Trochlear nerve

        d. Fifth cranial nerve- Trigeminal nerve

        e. Sixth nerve- Abducent nerve

        f. Sympathetic and parasympathetic nerve plexus.

STAGES OF ORBITAL INFECTIONS

PRESEPTAL CELLULITIS:

This is due to infection of the subcutaneous tissue of the eyelid anterior to the orbital septum. Due to loose attachment of connective tissue, the oedema caused by cellulitis in one eye easily spreads to the fellow eye.

Symptoms and signs:

1. Eyelid oedema
2. Erythema
3. Localised tenderness
4. Severe inflammation, but the globe is uninvolved
5. Pupillary reaction is normal
6. Visual acuity is normal
7. Ocular motility are not disturbed

Painful ophthalmoplegia and chemosis are absent. This is also called preorbital cellulitis. CT finding shows swelling of soft tissues of eyelid and structures near the orbital septum. Systemic antibiotics either oral or intravenous route is preferred. Non steroidal anti-inflammatory drug is also given. There is complete resolution of infection.

ORBITAL CELLULITIS:

This is due to infection posterior to the orbital septum. More commonly, this occurs as a secondary extension of acute or chronic sinusitis. It has got a potentially devastating consequence. Main clinical findings include

1. Hyperpyrexia
2. Leukocytosis
3. Proptosis which is irreducible and axial
4. Marked chemosis
5. Ptosis and
6. Painful ophthalmoplegia.
7. Decreased visual acuity
8. Defective colour vision
9. Restricted visual fields
10. Relative afferent pupillary defect

Compressive optic neuropathy demands immediate investigation and aggressive management. Heart rate, blood pressure, temperature and any signs of altered sensorium has to be monitored properly for these patients.

LABORATORY INVESTIGATIONS:

1. Total count and differential count shows leucocytosis

2. Erythrocytic sedimentation rate is elevated

3. Blood culture to isolate the organism

4. Nasopharyngeal culture

5. CSF analysis if there is central nervous system involvement.

    a. Pleocytosis

    b. Increased protein

    c. Increased sugar

Imaging is done before undertaking any surgical procedure.

X ray orbit, with different radiological views

1. Waters view
2. Caldwell view,
3. Rhese view
4. Lateral view

They are useful in visualising the opacification of Para nasal sinuses, thickening of mucosa, fluid levels in orbit. Ultrasonography reveals swelling of orbital tissues which is diffuse. There is widening of echogram of orbital fat with high reflectivity. CT shows invoivement of both intraconal and extraconal compartment. There will be proptosis and

obliteration of shadows of soft tissues. Thickening of soft tissues and optic nerve is seen. Debridement of sinuses is done in case of fungal sinusitis.

Intensive broad spectrum antibiotics through intra venous route have to be started and continued for two weeks followed by oral antibiotics for four weeks. In case of fungal infection, systemic anti-fungal therapy is started and associated metabolic abnormalities have to be corrected. Non-steroidal anti-inflammatory drugs, anti-pyretic therapy and rehydration have to be started.

SUBPERIOSTEAL ABSCESS:

This is due to inflammation between the bone and the periosteum and pus gets collected between these structures. Patients present with

1. Visual loss
2. Proptosis
3. Ophthalmoplegia.

Radiological investigations have to be done to confirm the diagnosis. A well outlined lesion located adjacent to the orbital wall which is demarcated from the orbital soft tissue by the highly reflective periosteum is suggestive of subperiosteal abscess. B scan shows fusiform appearance in longitudinal orientation. Fluid in the subperiosteal space shows low reflectivity. Treatment is similar to that of orbital cellulitis. Drainage of the abscess is through external or endonasal approach.

ORBITAL ABSCESS:

If orbital cellulitis is not intervened at appropriate time, it may progress to abscess formation within the orbital cavity. This is known as orbital abscess.

Patient presents with,

1. Proptosis
2. Chemosis
3. Visual loss
4. Complete ophthalmoplegia

Fundus examination reveals the presence of disc oedema and central retinal vein occlusion. Complications include intracranial spread leading to meningitis, intra cranial abscess and cavernous sinus thrombosis. Leucocytosis will be present and blood culture has to be done. MRI is more reliable than CT in diagnosing the intracranial spread. Ultrasonography is a useful adjunct. It shows low to medium reflective lesion which may appear solitary or multiloculated .Follow up scans taken after intense antibiotic therapy shows resolution of the previously identified lesions. Fine needle aspiration cytology is done to confirm diagnosis.

Aggressive parental antibiotics with judicious surgical intervention constitute the main stay of treatment. Empirical treatment of proptosis with systemic steroids should be avoided as it aggravates the infection.

CAVERNOUS SINUS THROMBOSIS:

It is the septic thrombosis of the cavernous sinus. Starts unilaterally but soon becomes bilateral.

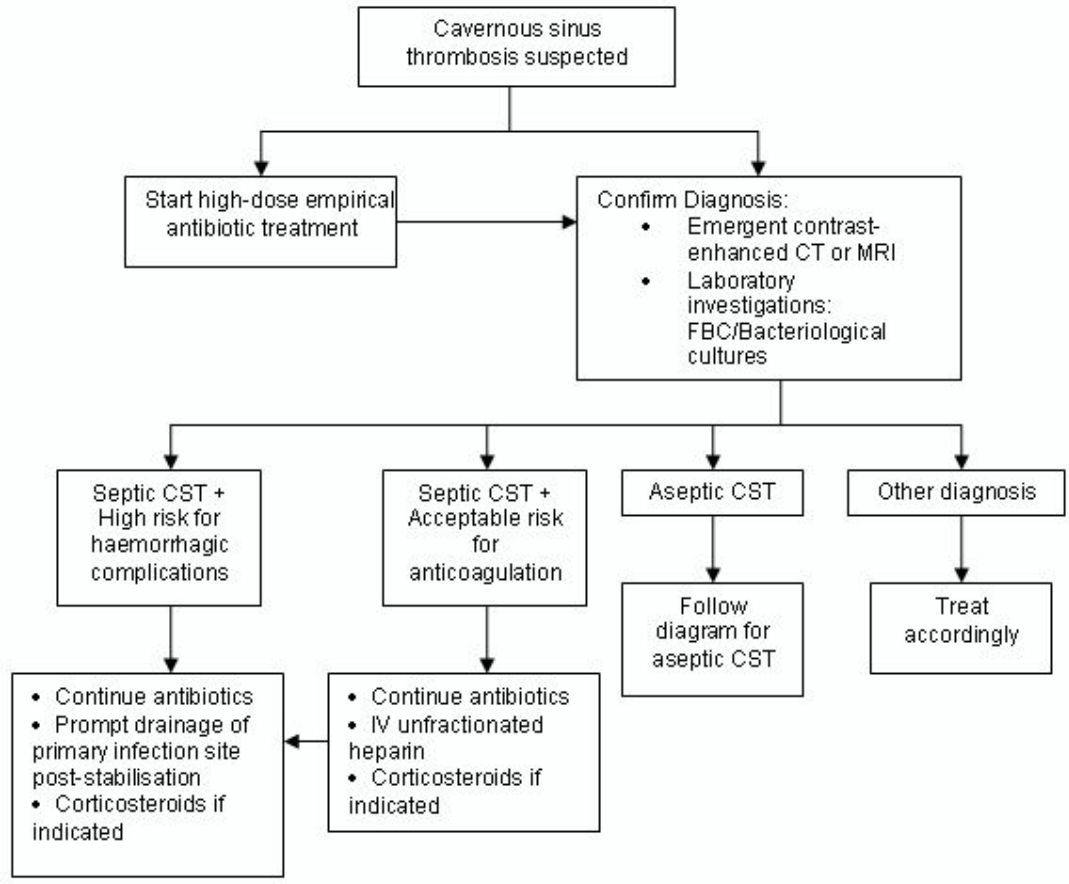
Patients present with,

1. Moderate proptosis
2. Painful ophthalmoplegia
3. Multiple cranial nerve palsy
4. Oedema of mastoid region due to back pressure in mastoid emissary veins.

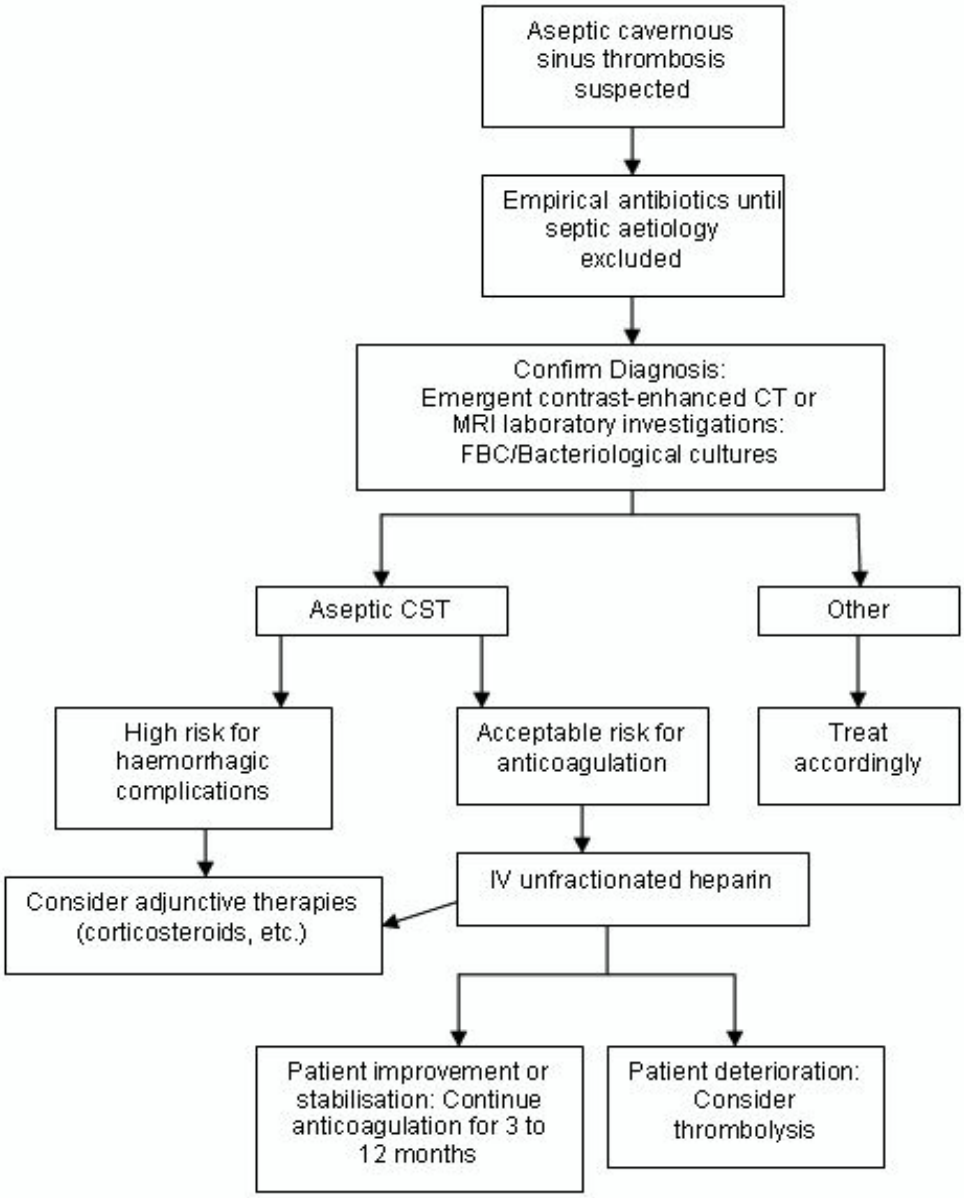
The retinal veins are congested and disc oedema is present. Decreased level of consciousness, confusion, seizures and focal neurological deficit indicate CNS spread. Non contrast CT reveals high density thrombus in the affected cavernous sinus. Contrast enhanced CT shows distension of the cavernous sinus with non-fat density filling defect with distension of the bilateral superior ophthalmic veins. MRI shows absent flow void and the signal characteristics vary with the age of thrombus but will be abnormal. Mainly routine T2, Fluid Attenuated Inversion Recovery and pre contrast and post contrast T1 weighted less than 3mm thick images in both axial and coronal planes are useful in clinching the diagnosis. MR Venography will reveal the exact site of the thrombus. Broad spectrum antibiotics which cover both gram positive and gram negative organism are used. Sphenoidal abscess has to be drained.

MANAGEMENT PROTOCOL FOR CAVERNOUS SINUS THROMBOSIS

FLOW CHART 1:



FLOW CHART 2:


Aseptic cavernous sinus thrombosis suspected
Empirical antibiotics until septic aetiology excluded
Confirm Diagnosis: Emergent contrast-enhanced CT or MRI laboratory investigations: FBC/Bacteriological cultures
Aseptic CST
Other
High risk for haemorrhagic complications
Acceptable risk for anticoagulation
Treat accordingly
Consider adjunctive therapies (corticosteroids, etc.)
IV unfractionated heparin
Patient improvement or stabilisation: Continue anticoagulation for 3 to 12 months
Patient deterioration: Consider thrombolysis

CLASSIFICATION OF FUNGI

Fungi are ubiquitous organisms found in soil and decaying organic matters. They lack chlorophyll and in contrast to bacteria, cell membranes of fungi are rich in ergosterol. They are generally saprophytes but become pathogens to cause opportunistic infection when there is decline in the local and systemic immunity. Fungal infections cause serious ocular infection with potentially catastrophic visual results.

As per morphology, the fungi are classified into four main classes:

1. YEAST

   Cryptococcus

2. YEAST LIKE FUNGI

   Candida

3. DIMORPHIC FUNGI

   Histoplasmosis

   Coccidioides

   Sporotrix

   Blastomycetes

4. FILAMENTOUS FUNGI

Filamentous fungi are sub classified into septate and nonseptate fungi. The septate fungi are further divided into pigmented and non pigmented types.

SEPTATE FUNGI

NON PIGMENTED

1. Fusarium
2. Aspergillus
3. Acremonium
4. Pencillium
5. Petricillidium boydii
6. Geogrichum
7. Myrathecum
8. Vollutella
9. Cylindro Carpon

PIGMENTED

1. Curvularia
2. Cladosporum
3. Alternaria

4. Sphaerosidalupes
5. Drechslera
6. Philalophora
7. Melanconliaces

NON SEPTATE

1. Mucor
2. Rhizopus
3. Absidia

YEASTS

These are unicellular spherical organisms that multiply mainly by budding. The only pathogenic yeast is Cryptococcus neoformans which cause fungal meningitis. Rarely does it cause endogenous endophthalmitis.

YEAST LIKE FUNGI

Some of them develop partly as yeasts and others by pseudomycellia which are chains of elongated budding cells joined end to end. E.g. Candida albicans.

MOULDS

These are mycelial or filamentous fungi. Most comprise of cylindrical branches called hyphae. Entangled masses of hyphae are called mycelium.

DIMORPHIC FUNGI:

These fungi assume two different forms at different temperature in soil and in culture. They are moulds, but in host body they appear like yeasts. Most of the fungi causing systemic infections are dimorphic. Eg, Coccidioides, Histoplasma

MODES OF REPRODUCTION OF FUNGI:

The fungi can reproduce in three ways, i.e., asexually, sexually and combined mode. The spores are the reproductive part in fungi. The asexual spores are called conidiospores. On the basis of spore formation, fungi can be divided into four classes:

1. Phycomycetes
2. Ascomycetes
3. Basidiomycetes
4. Deuteromycetes

MYCOLOGY:

Mucorales are subset of the phycomycetes. Within the mucorales, the genera most commonly responsible for human rhino-orbital mucormycosis are Rhizopus, Mucor, Absidia, and recently identified Apophysomyces.

Common species

Rhiopus oryzae

Rhizopus microsproreus

Absidia corymbifera

Commonly, immunocompromised are affected because when the PH is very low, serum cannot bind iron effectively. High iron content and glucose rich milieu facilitate fungal growth. The fungal hyphae have the ability to produce rhizoferrin that easily binds with iron and forms a complex which is utilized by the fungus for its important metabolic activities. Phagocytic and chemotactic properties of neutrophils in diabetic patients are ineffective. Therefore, they are highly predisposed to fungal infections like mucormycosis. Moreover in diabetes, acidosis and hyperglycemia favour increased growth of fungi.

Phycomycetes are ubiquitous saprophytic fungi that are not pathogenic to human being. After inhalation, the spores are rapidly eliminated by phagocytosis and oxidative killing by macrophages.

Clinical presentation of mucormycosis

a. Rhinocerebral
b. Pulmonary
c. Gastrointestinal
d. Central nervous system
e. Subcutaneous
f. Disseminated

ORBITAL FUNGAL INFECTIONS:

There are two main classes of fungal infections

1. Mucormycosis
2. Aspergillosis

ORBITAL MUCORMYCOSIS:

It is a virulent fungal disease of orbit caused by species of rhizopus, belonging to class Zygomycetes.

It is seen predominantly in,

i. Debilitated and immune-compromised patients
ii. Uncontrolled diabetes mellitus
iii. Diabetic ketoacidosis
iv. Metabolic acidosis patients
v. Chemotherapy for haematological malignancies
vi. Renal failure
vii. Septicaemia
viii. Antecedent bacterial infection
ix. Alcoholic cirrhosis
x. Blood dyscrasia

The disease of orbit spreads to adjacent sinuses and brain. The infection gains entrance to the CNS through orbital roof and apex and through the cribriform plate. The fungal invasion of blood vessels (angioinvasion) cause occlusive thrombosing vasculitis by causing damage to the endothelium, tunica media and inner vascular layer, thereby causing platelet aggregation and formation of thrombus. Internal carotid artery, middle cerebral artery, ciliary arteries, retinal arteries as well as cavernous sinus are all subject to this process.

SYMPTOMS

1. Peri orbital pain
2. Retro orbital pain
3. Facial pain
4. Pharyngitis
5. Foul smelling seropurulent nasal discharge
6. Visual loss

The nasal cavity and paranasal sinuses of same side are involved. There can be loss of sense of smell and facial numbness. There is wide spread gangrene of the nasal mucosa accompanied by perforation of nasal septum and necrosis of the turbinate and palate. Generalised symptoms like fever, lethargy and headache will be present. The visual acuity is reduced. Proptosis and ptosis may be present. Signs of inflammation such as chemosis and congestion may be present in the involved eye. Multiple cranial nerve palsy involving the third, fourth, fifth, sixth and seventh cranial nerves may occur. Infections involving orbital apex will present with partial or total ophthalmoparesis (internal and external), periorbital

numbness secondary to trigeminal nerve involvement and optic nerve involvement with relative afferent pupillary defect. There can be localised tissue necrosis with black eschar in the nares and palate. In advanced disease there will be periocular and facial skin involvement too. Cerebral involvement often occurs by direct spread or haematogenous spread. The patient deteriorates rapidly into a condition of semi coma and death is frequently within a week.

MANAGEMENT:

INVESTIGATIONS:

Blood investigations show,

Elevated erythrocyte sedimentation rate

Increased white blood cell count

Blood culture is typically negative.

Computerised tomography shows a well circumscribed, homogenous or irregular soft tissue mass, seen in the orbit which extends to the adjacent Para nasal sinuses and spreads intracranially if not intervened at appropriate time. There can be bony erosions and later bony destruction, orbital displacement, exophthalmos and optic nerve enlargement. CT may also reveal venous filling defects suggestive of thrombosis.

Magnetic resonance imaging shows a thickened mucosa and obliteration of the sinus cavity with hyper intense signals on T2 weighted images. It also gives details about the intracranial extension of the infection, which may present as frontal lobe mass and carotid

artery invasion. MRI shows narrowing and occlusion of carotid arteries absence of flow in Superior ophthalmic veins.

Biopsy taken from affected tissue will show fungal filaments which appear as non septate, large, branching hyphae.

STAINING:

1. Haematoxylin and eosin
2. Periodic acid Schiff
3. Gomorri methenamine silver

It also shows fungal growth suggestive of rhizopus when inoculated in appropriate culture media. Sabouraud' dextrose agar at 37 degree Centigrade with antibiotics but without actidione is commonly used. The colonies were dense and had whitish appearance. A microscopic examination of the growth with lacto phenol cotton blue mount will reveal rhizopus. The material for biopsy can also be obtained by endoscopic approach. As mucormycosis is associated with underlying systemic conditions like diabetic ketoacidosis, haematologic malignancies, chronic renal failure and immunocompromised status, relevant investigations should be done to rule out these conditions.

TREATMENT:

Mucormycosis needs a multispeciality care from the orbital surgeon, neurosurgeon and the otolaryngologist for its treatment. Patients with rhino orbital mucormycosis need extensive and repeated debridement of sinuses, orbit and infected areas. The main aim is to

remove the unhealthy tissue. In case of severe orbital disease, exenteration of orbit is done as a lifesaving method in nearly half of the cases.

Mucormycosis is effectively treated by the following steps.

1. Diagnosis in time.
2. Identifying and reversing factors at risk
3. Debridement of necrotic tissues surgically
4. Timely initiation of drugs against fungal invasion

ANTI FUNGAL MEDICATIONS:

POLYENES:

Amphotericin B is the effective drug in the treatment of mucormycosis. Nephrotoxicity is significantly reduced if Amphotericin lipid formulations are used. These kind of modified medications are safe and they can be used for longer duration when compared to Amphotericin B. A recent retrospective series showed that in patients with rhino orbital cerebral mucormycosis, treatment outcomes were inferior when amphoterin B lipid complex was given as first line of treatment compared with amphotericin B or liposomal amphotericin B.

AZOLES:

Drugs like voriconazole and fluconazole are ineffective as primary drug therapy in the treatment of mucormycosis. Absidia is mainly treated with itraconazole, whereas mucorales are effectively handled with posaconazole, with 90% MIC of 1 to $\geq$ 4 microgram/ml.

Posaconazole was found to be inferior to Amphotericin B in treating murine disease as showed by studies from four groups. It also did not have any superior effect when compared to placebo in a study conducted by three more groups on treating mucormycosis in mice. Therefore it can be inferred that though posaconazole cannot be used as first line management in mucormycosis, it can still be considered as an option for polyene intolerance or refractoriness.

Systemic anti-fungal like intravenous amphotericin B, at a dose of 1 to 1.5mg/kg/day is suggested in the acute phase of the disease. Treatment is generally prolonged. The effectiveness of treatment is increased by the use of liposomal amphotericin B at a dose of 3-10mg/kg/day. Lipid encapsulated antifungal drugs permits cumulative dose with reduced level of toxicity. Newer antifungal therapy with posaconazole and voriconazole are effective against rhizopus. Adjunctive treatments, including hyperbaric oxygen, local infusion of Amphotericin B and GM-CSF therapy may play an increasing role in future. Concurrent systemic condition needs supportive therapy.

COMBINATION ANTIFUNGAL THERAPYS:

ECHINOCANDINS:

Studies have shown that in DKA mice infected with Rhizopus oryzae, a combination therapy of caspofungin plus Amphotericin B lipid complex prolonged and improved survival remarkably. Similarly, there are few results showing improved outcome in DKA mice with disseminated mucormycosis when a combination of Liposomal Amphotericin B and either micafungin or anidulafungin was used. The reason for this improved outcome may be attributed to immune stimulation that results from increased exposure of beta glucan on the surface of the fungus.

In a recent trial conducted on patients with rhino orbital cerebral mucormycosis, combination of LFAB and caspofungin produced measurable positive outcomes compared with polyene alone.

IRON CHELATION THERAPY:

Desferrioxamine increase delivery of iron to the fungal elements thereby enhancing their growth. Hence, iron chelation therapy predisposes to mucormycosis. However there are agents other than desferrioxamine that cause chelation of iron and at the same time cannot be used by the mucorales to utilize iron for their growth. Such an agent called deferasirox, which was used for the treatment of iron overload in transfusion dependent anaemia's, was found to be effective in killing fungal elements of mucorales in vitro. Research has shown that deferasirox was as effective as LAMB therapy in DKA mice with disseminated fungal disease.

OTHER ADJUNCTIVE THERAPIES:

Cytokines which are responsible for causing inflammation like IFN and GM-CSF possess the ability to destroy mucorales by increasing the ability of granulocytes. Those cases of mucormycosis which do not respond to regular treatment can be treated with Granulocyte macrophage colony stimulating factor, especially in patients with neutropenia as a life saving measure. Latest evidence indicates that hyperbaric oxygen increases the antifungal activity of neutrophils and oxidative killing mechanism of polyenes.

ROLE OF SURGERY:

The characteristic angio-invasiveness of the fungi results in the formation of thrombotic tissue infarction and necrosis that prevent the antifungals from efficient

penetration of the infected area. Timely debridement if possible, of all the devitalised tissue appears reasonable in order to reduce the mass of infecting moulds and to stop invasion into adjacent structures. Studies indicate the importance of timely surgical intervention in orbital mucormycosis, if needed, by the way of exenteration, resection, orbital lateral rhinotomy, mandibulectomy or craniotomy to improve survival rate. Impaired drug delivery to the affected area because of thrombosis in the vascular lumen and limitation of any surgical procedure due to the complex anatomy of orbit and nasal cavity, complications associated with the disease and presentation at a later date, account for high residual morbidity & mortality rates.

PROGNOSIS:

Rhino orbital phycomycete infection has a poor prognosis with delayed diagnosis or treatment. Following introduction of amphotericin B mortality rate has fallen from 90% to 30%, although higher mortality rate has been reported in isolated pulmonary mucormycosis and in those with intracranial extension. The low survival rate is not only due to the aggressive nature of Mucor and Rhizopus, but also failure to consider the diagnosis in the context of debilitated patient receiving treatment for other life threatening conditions.

PART II

AIMS AND OBJECTIVES

1. To analyse the various clinical presentation of orbital mucormycosis in diabetes mellitus
2. To establish the importance of preventing case fatality and reducing ocular morbidity through early diagnosis and prompt management.

STUDY DESIGN

Prospective non comparative interventional analytical cohort study.

METHODS AND METHODOLOGY

INCLUSION CRITERIA

1. Age >40yrs
2. Type II Diabetes Mellitus
3. Histopathologically confirmed diagnosis of Mucormycosis
4. Similar treatment strategy of systemic antifungal therapy followed by surgical debridement and adjuvant treatment.

EXCLUSION CRITERIA

1. Age <40yrs
2. Juvenile/ Type I Diabetes Mellitus

3. Other associations of orbital mucormycosis like

    a. Malignant haematological disorders

    b. Chronic renal failure, metabolic acidosis,

    c. Prolonged glucocorticoid or desferoxamine therapy

4. Participants who discharged themselves against medical advice and lost to follow up.

MATERIALS AND METHODS

This prospective study was conducted in RIO GOH, Egmore, Chennai for a period of 12 months.

30 patients were selected based upon the inclusion criteria.

Patients were admitted and evaluated clinically and radiologically.

PATIENT EVALUATION

1. Detailed history was elicited.

    - Duration of illness
    - Mode of onset
    - Associated symptoms
    - Prior history of medical and surgical treatment

2. General examination

    - Anemia
    - Jaundice
    - Clubbing
    - Lymphadenopathy
    - Pulse, BP, Respiratory rate, Temperature

3. Ophthalmic Evaluation

    - Visual acuity using Snellen's chart
    - Examination of orbit and adnexa
    - Direct and Indirect ophthalmoscopy
    - Colour vision
    - Hertels exophthalmometry
    - IOP measurement using Goldmann Applanation Tonometer
    - Diplopia charting and visual field charting
    - B scan ultrasonography/X-ray orbit/CT scan/ MRI
    - Tissue biopsy /orbital FNAC

4. Laboratory Investigations

    - Routine blood investigations
    - Fasting and Post prandial blood sugar
    - Urine sugar and ketone bodies
    - Blood gas analysis

The patients were also referred to E.N.T department, Neurology, Physician and Dental surgeon for their expert opinion in aiding the diagnosis and management.

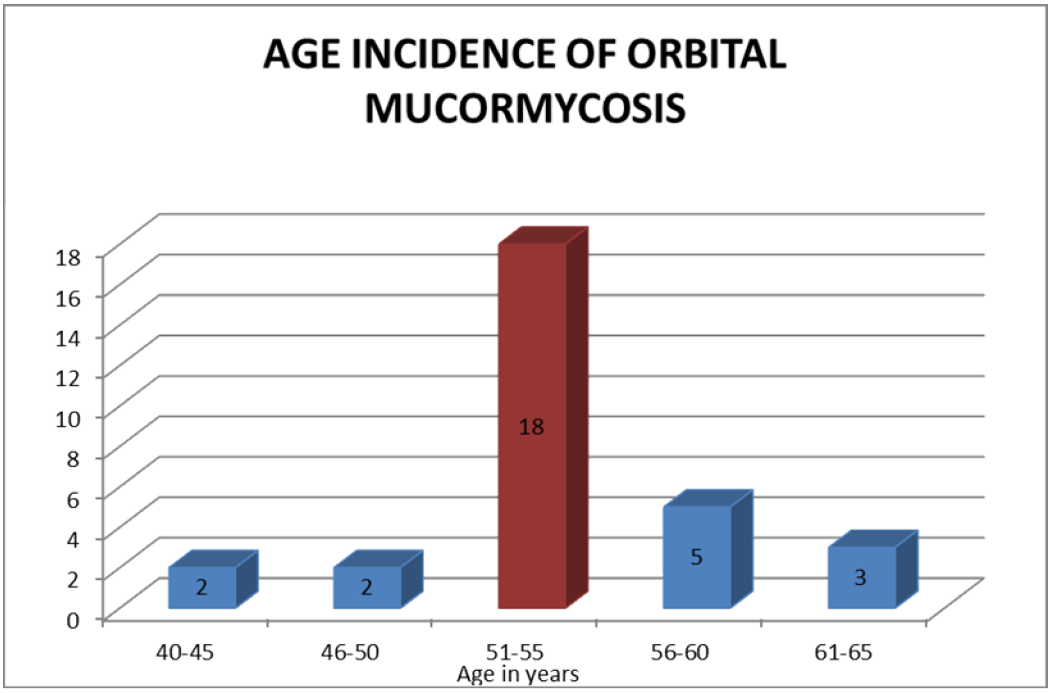
All the patients were given similar medical and appropriate surgical therapy and closely monitored for changes in the subjective symptoms and objective signs throughout the treatment period. Patients will be followed up at 1, 4, 6 weeks and 3, 6, 12 months. On each follow up visit, visual acuity, slit lamp examination, IDO, IOP measurement will be recorded and also assessed for development of possible complications which will be managed accordingly.

OBSERVATION AND RESULTS

TABLE-1: AGE INCIDENCE OF ORBITAL MUCORMYCOSIS

AGE GROUP	INCIDENCE	PERCENTAGE
40-45	2	6.67
46-50	2	6.67
51-55	18	60
56-60	5	16.67
61-65	3	10

CHART 1:

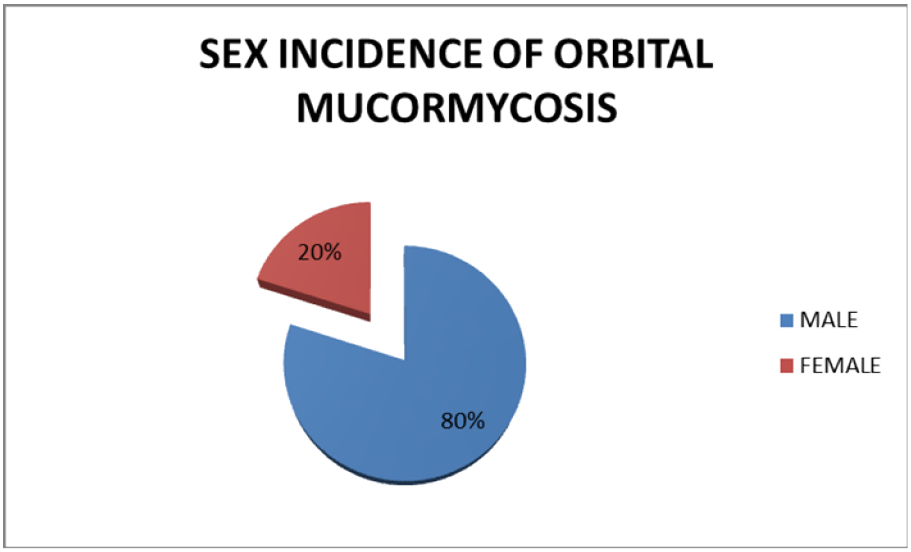


Of the thirty patients in our study, majority of patients (18) were in 50-55 years age group, 5 were in 55-60 years age group,3 were in 60-65 years age group and 2 were in age group 45-50 and remaining 2 in 40-45 years. Persons above fifty years of age are the most affected because of their increased susceptibility to infections.

TABLE 2: SEX INCIDENCE OF ORBITAL MUCORMYCOSIS

SEX	INCIDENCE	PERCENTAGE
MALE	24	80
FEMALE	6	20

CHART 2:

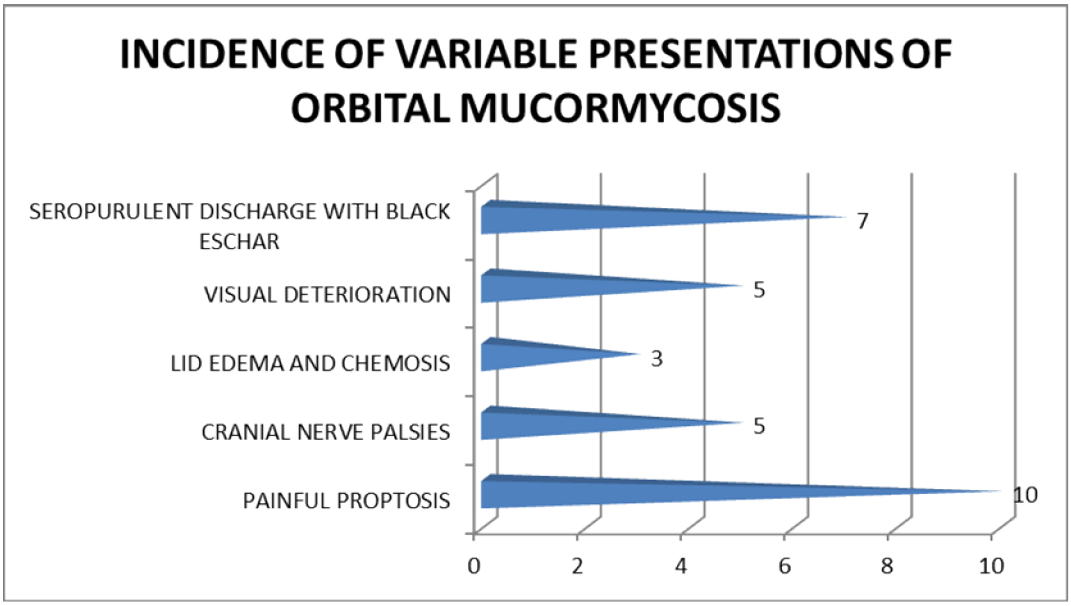


Eighty percentage of the study subjects are males and the remaining 20% are females.

TABLE-3: INCIDENCE OF VARIABLE PRESENTATION OF MUCORMYCOSIS OF ORBIT

CLINICAL PRESENTATION	NUMBER OF PATIENTS	PERCENTAGE
SEROPURULENT DISCHARGE WITH BLACK ESCHAR	7	23.33
VISUAL DETERIORATION	5	16.67
LID EDEMA AND CHEMOSIS	3	10
CRANIAL NERVE PALSIES	5	16.67
PAINFUL PROPTOSIS	10	33.33

CHART 3:

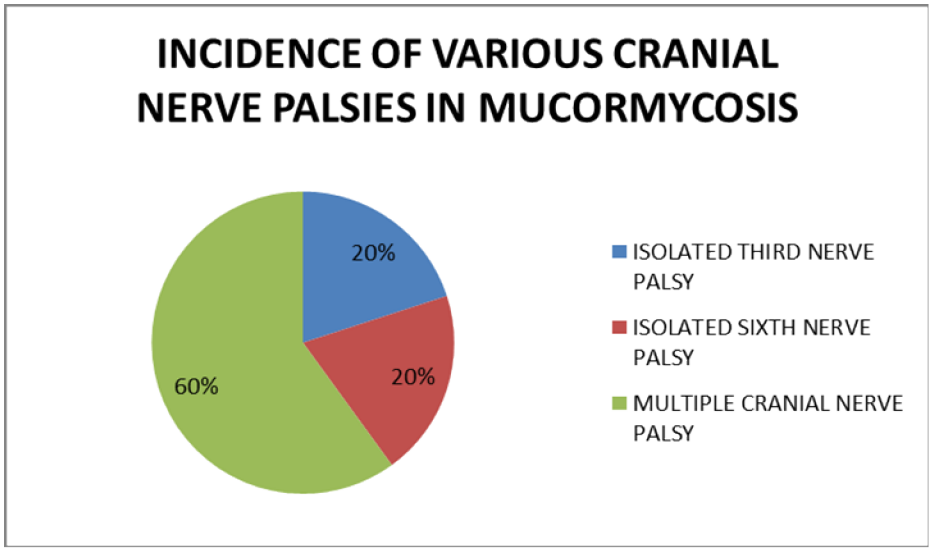


Ten among the thirty patients (33%) came with painful proptosis at the time of presentation. This was the most common mode of presentation. Seven patients (23%) presented with seropurulent discharge with black eschar. Very few presented with defective vision (17%), lid oedema, chemosis (10%) and cranial nerve palsies (17%).

TABLE 4: INCIDENCE OF VARIOUS CRANIAL NERVE PALSIES IN MUCORMYCOSIS

NERVE PALSY	NUMBER	PERCENTAGE
ISOLATED THIRD NERVE PALSY	1	20
ISOLATED SIXTH NERVE PALSY	1	20
MULTIPLE CRANIAL NERVE PALSY	3	60

CHART 4:

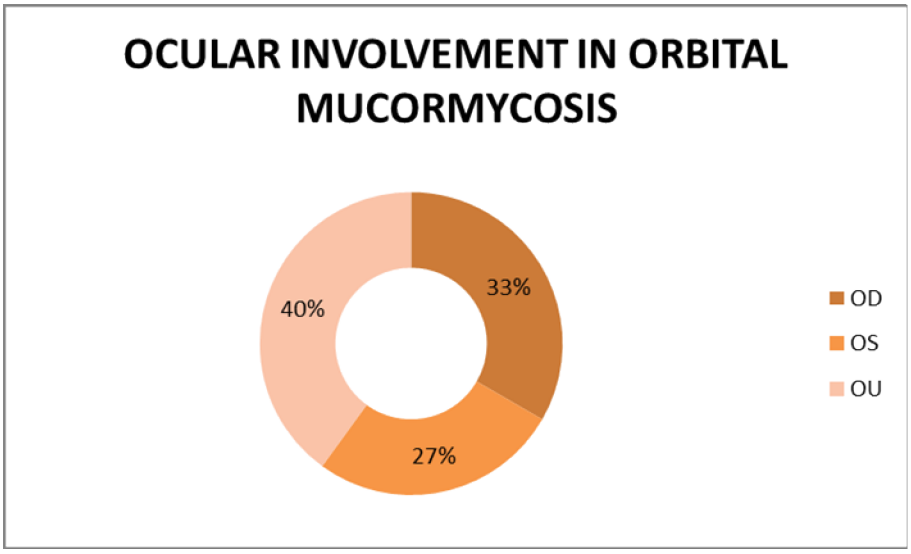


In our study, the involvement of multiple cranial nerves (60%) was more commonly observed than isolated cranial nerve palsies.

TABLE 5: OCULAR INVOLVEMENT IN ORBITAL MUCORMYCOSIS

EYE INVOLVED	NO. OF PATIENTS	PERCENTAGE
OD	10	33.33
OS	08	26.67
OU	12	40.00

CHART 5:

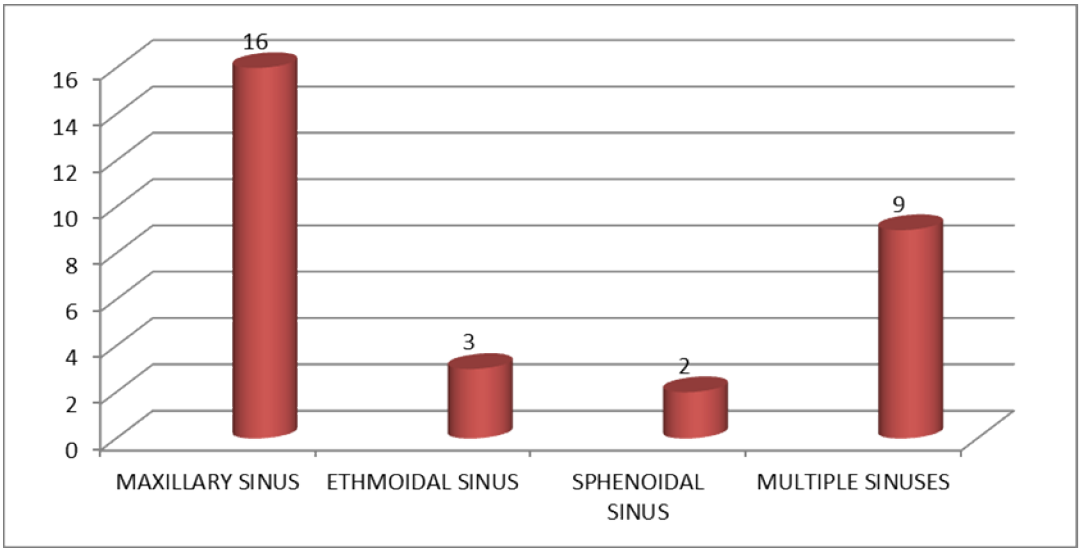


Most of the patients with mucormycosis had bilateral involvement (40%). The involvement of right eye was more than left eye.

TABLE 6: PATTERN OF SINUS INVOLVEMENT IN ORBITAL MUCORMYCOSIS

SINUS INVOLVEMENT	NO. OF PATIENTS	PERCENTAGE
MAXILLARY SINUS	16	53.33
ETHMOIDAL SINUS	3	10.00
SPHENOIDAL SINUS	2	6.67
MULTIPLE SINUSES	9	30.00

CHART 6:

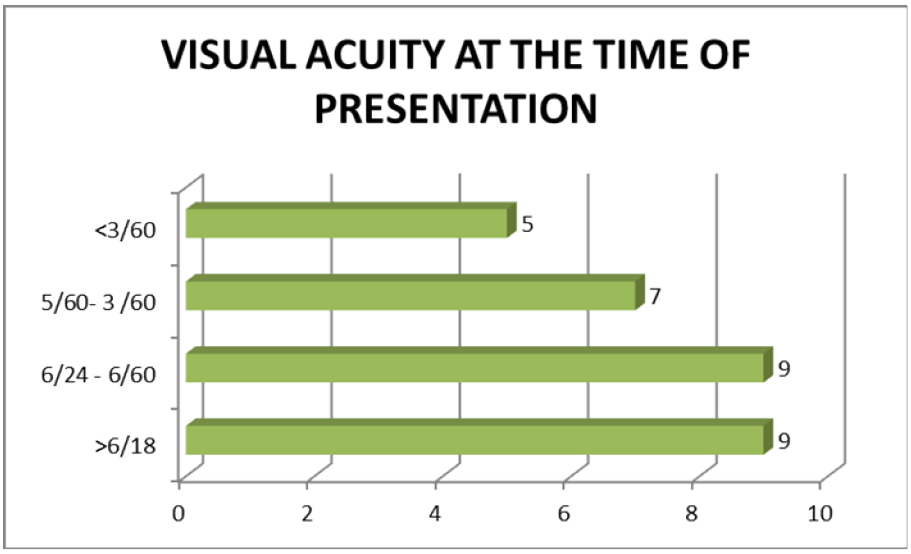


Maxillary sinus (16%) was the most commonly affected, followed by multiple sinus involvement (9%). Very few had involvement of ethmoidal and sphenoidal sinuses.

TABLE 7: VISUAL ACUITY AT THE TIME OF PRESENTATION

VISUAL ACUITY	NUMBER OF PATIENTS	PERCENTAGE
> 6/18	9	30
6/24 – 6/60	9	30
5/60 – 3/60	7	23.33
< 3/60	5	16.67

CHART 7:

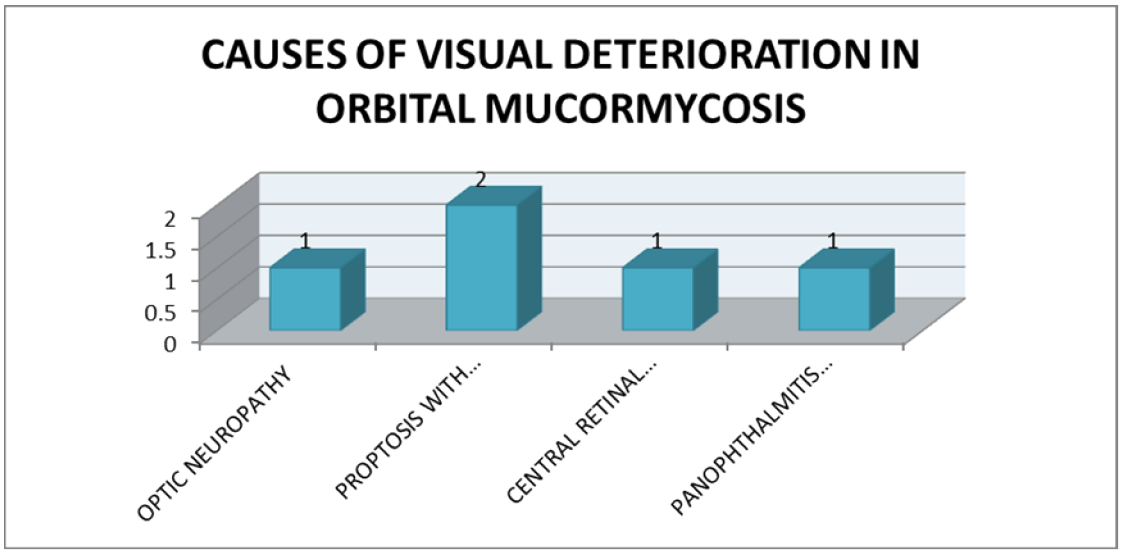


Though all the patients presented with diminished visual acuity, only 16% (5 out of 30) had a visual acuity of less than 3/60 and 23% (7 out of 30) had a visual acuity between 5/60 – 3/60. 30% of the study group had quite a good visual acuity of around 6/60 – 6/24. Another 30% had greater than 6/18 vision. This chart infers that most of the patients who presented to the OPD had a near normal vision.

TABLE 8: CAUSES OF VISUAL DETERIORATION IN ORBITAL MUCORMYCOSIS

CAUSE OF VISUAL DETERIORATION	NUMBER	PERCENTAGE
OPTIC NEUROPATHY	1	20
PROPTOSIS WITH EXPOSURE KERATOPATHY	2	40
CENTRAL RETINAL VEIN OCCLUSION	1	20
PANOPHTHALMITIS WITH CORNEAL MELTING	1	20

CHART 8:

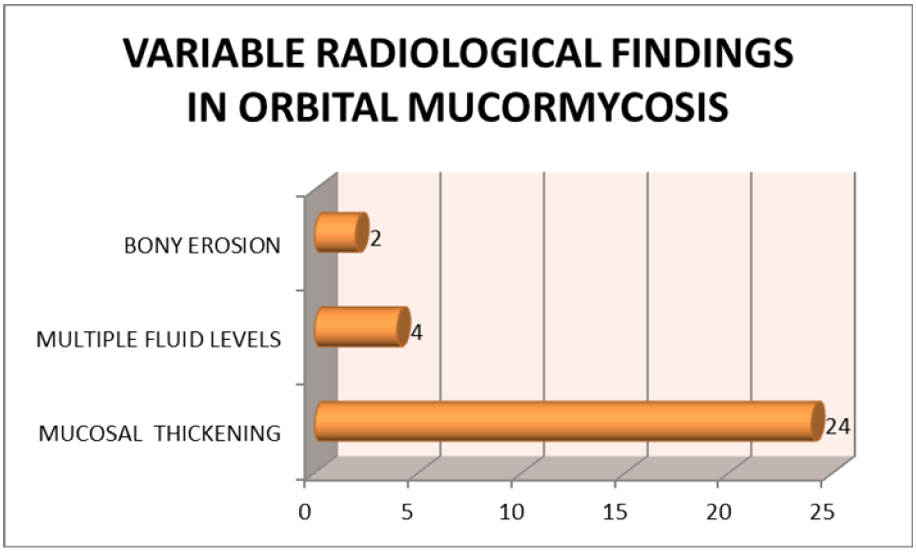


The common causes of visual deterioration in mucormycosis were optic neuropathy, proptosis with exposure keratitis, central retinal vein occlusion and panophthalmitis. Among these, exposure keratopathy (40%) was the most frequently observed cause of diminished vision. Other evaluated causes had an equal contribution to visual deterioration.

TABLE 9: VARIABLE RADIOLOGICAL FINDINGS IN ORBITAL MUCORMYCOSIS

RADIOLOGICAL FINDING	NUMBER OF PATIENTS	PERCENTAGE
MUCOSAL THICKENING	24	80
MULTIPLE FLUID LEVELS	4	13
BONY EROSION	2	6

CHART 9:



CT orbit of the patients showed mucosal thickening in 24% of the study group whereas mutiple fluid levels in the orbit were found in 4% and bony erosions in just 2%.

CHART 10:

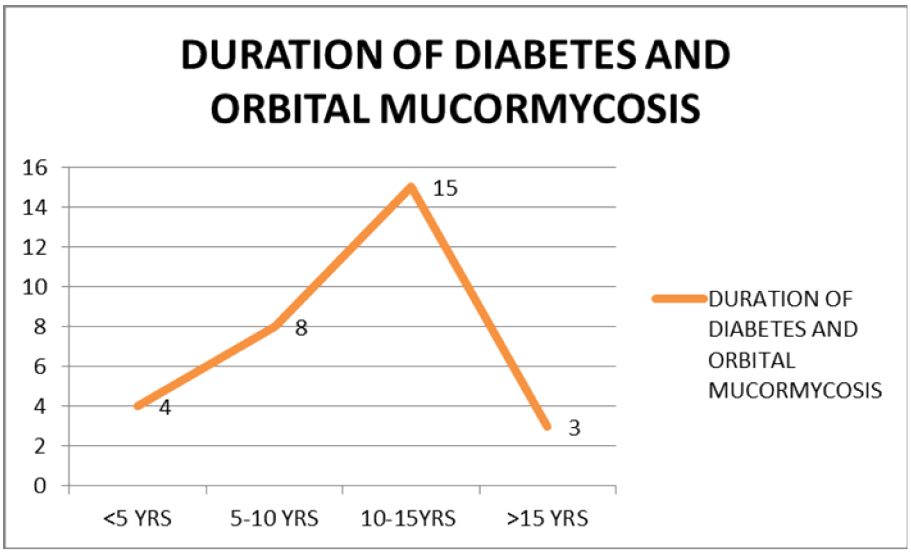


TABLE 10: DURATION OF DIABETES AND ORBITAL MUCORMYCOSIS

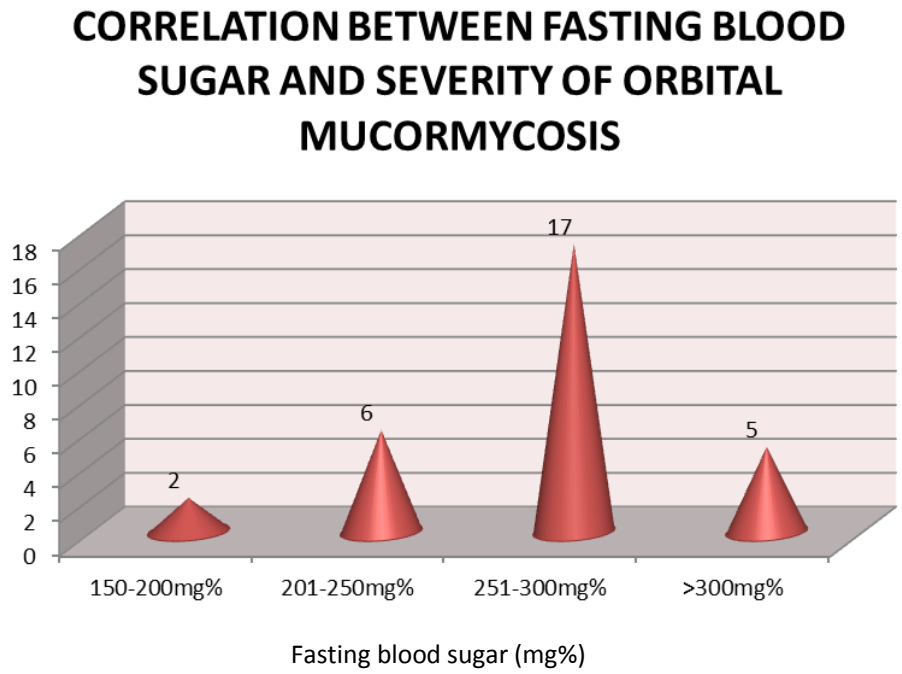
DURATION OF DIABETES	NUMBER OF PATIENTS	PERCENTAGE
<5 YEARS	4	13.33
6 – 10 YEARS	8	26.67
11 – 15 YEARS	15	50
>15 YEARS	3	10

In our study, 50% of the patients who presented with mucormycosis were known diabetics for about 10 – 15 years. 27% were found to be diabetics with a duration of eight years and 13% with a duration of less than five years. Since the survival rate of patients with type 2 diabetes mellitus for greater than 15 years duration is decreased due to other associated systemic complications in a developing country like ours, we find few cases of mucormycosis in such criteria

TABLE 11: CORRELATION BETWEEN FASTING BLOOD SUGAR AND SEVERITY OF ORBITAL MUCORMYCOSIS

FASTING BLOOD SUGAR	NUMBER OF PATIENTS	PERCENTAGE
150 – 200 mg%	2	6.67
201 – 250 mg%	6	20.00
251 – 300 mg%	17	56.67
>300 mg%	5	16.67

CHART 11:

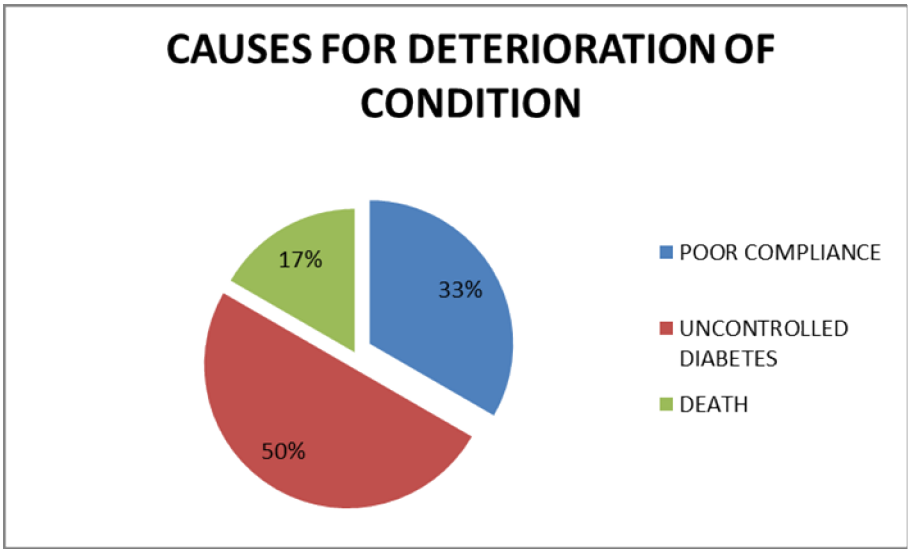


Patients with uncontrolled fasting blood sugar levels (250 – 300 mg/dl) were the most common to suffer from aggressive mucormycosis (17%). This is found to decrease with decrease in the value of fasting blood sugar level. On the other hand, we had only five patients who presented with a fasting blood sugar level of greater than 300 mg/dl. This may be due to the fact that at such high levels of blood glucose, as the scenario in a developing nation like ours, patients may have to succumb to their illness.

TABLE 12: CAUSES FOR DETERIORATION OF CONDITION

CAUSES	NUMBER OF PATIENTS	PERCENTAGE
POOR COMPLIANCE	2	33.33
UNCONTROLLED DIABETES	3	50.00
DEATH	1	16.66

CHART 12:

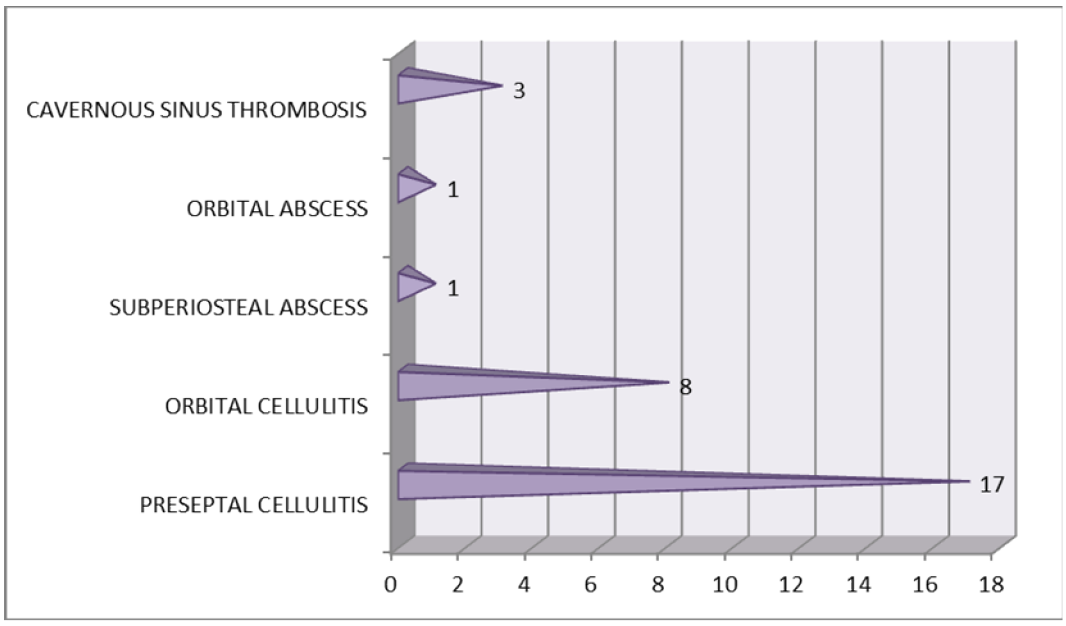


As recorded in our study, uncontrolled diabetes (50%) was the most common cause for deterioration of the general condition of the patient, followed by poor compliance (33%) to treatment and death (17%).

TABLE 13: VARIED ORBITAL MANIFESTATION OF MUCORMYCOSIS

ORBITAL MANIFESTATION	NUMBER OF PATIENTS	PERCENTAGE
PRESEPTAL CELLULITIS	17	56.67
ORBITAL CELLULITIS	8	26.67
SUBPERIOSTEAL ABSCESS	1	3.33
ORBITAL ABSCESS	1	3.33
CAVERNOUS SINUS THROMBOSIS	3	10.00

CHART 13:

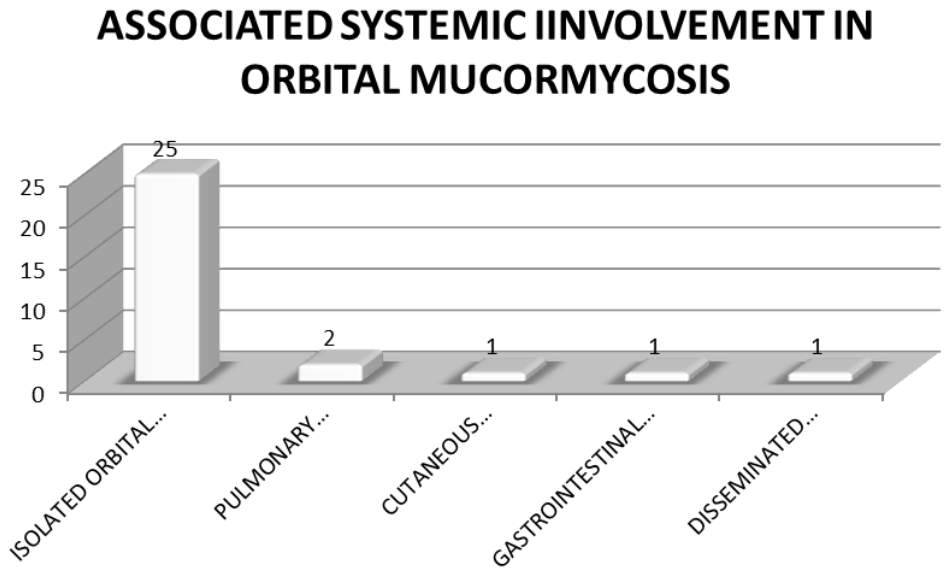


In our study, pre septal cellulitis (67%) was the most common orbital manifestation of mucormycosis followed by orbital cellulitis (17%) and cavernous sinus thrombosis (10%). Very few had a sub periosteal or an orbital abscess.

TABLE 14: ASSOCIATED SYSTEMIC INVOLVEMENT IN ORBITAL MUCORMYCOSIS

SYSTEMIC ASSOCIATION	NUMBER OF PATIENTS	PERCENTAGE
ISOLATED ORBITAL MUCORMYCOSIS	25	83.33
PULMONARY MUCORMYCOSIS	2	6.67
CUTANEOUS MUCORMYCOSIS	1	3.33
GASTROINTESTINAL MUCORMYCOSIS	1	3.33
DISSEMINATED MUCORMYCOSIS	1	3.33

CHART 14:



83% of the patients presented with isolated orbital mucormycosis. Those with associated systemic illness like pulmonary, cutaneous, gastrointestinal and disseminated disease was less than 10%..

DISCUSSION

A study conducted by Maureen M .Roden et al, states that there is increased prevalence of zygomycosis in male population when compared to female population which supports our study in which male patients out number the female. Lanternier et al, study also explains the same. A paper submitted in University of Wale's Institute Cardiff shows similar data in age group in par with our study.

This study also tells that, diabetics are more prone for orbital mucormycosis and uncontrolled blood sugar is important etiological factor which predispose to this condition. The infection spreads mainly through the sinuses and involvements of various sinuses are documented in our study.

Variable presentations of zygomycosis are studied, and found isolated rhino- orbital-mucormycosis is commonest of all, which is proved in our study. As per George Petrikkos et al, various symptoms and signs in mucormycosis were studied and causes of visual deterioration were identified. Early intervention decreased the ocular morbidity and mortality of the affected individual which is similar to our study.

The commonest presentation in our study was painful proptosis, followed by seropurulent discharge with black eschar. Patient presenting with lid oedema and chemosis, cranial nerve palsies and defective vision are less.

60 percent of our study group had multiple cranial nerve involvement. Bilateral involvement is more common (40 percent) but asymmetrical .Maxillary involvement is the commonest sinus to be involved followed by multiple sinus involvement. In the study by E

lgin K Weiss A, et al the ratio of sinusitis accompanying orbital infection was 90 percent which is seen in our study.

Even though decreased visual acuity was found at the time of presentation, only 16 percent had visual acuity less than 3/60.Causes of deterioration of vision showed 40 percent in patients with proptosis with exposure keratopathy. Other causes like optic neuropathy, central retinal vein occlusion and panophthalmitis were 20 percent.

Higher incidence of mucormycosis were found in population with 6-10 years duration of diabetes (27 percent).Patients with uncontrolled fasting blood sugar level(250-300 mg/dl) were the most common to suffer from aggressive mucormycosis. According to Ravindra et al in 2013 and M oht Hayat et al, this life threatening infection is common among patients with high blood sugar level. Ghana Technology University College has submitted a paper with similar data, in duration of diabetes and mucormycosis which supports our study.

The most common orbital manifestation of mucormycosis is preseptal cellulitis (67 percent) .Next to this is orbital cellulitis which was 27 percent and cavernous sinus thrombosis which was 10 percent.83 percent of the patient in our study presented as an isolated orbital mucormycosis and only less than 10 percent was with systemic involvement.

SUMMARY

The study aimed at analysing the various clinical presentations of Orbital mucormycosis in diabetes. The study also establishes the importance of reducing the ocular morbidity through early diagnosis and prompt management.

The study was conducted in Regional institute of Ophthalmology, Chennai which included 30 patients. Patients of age group more than 40 and known case of diabetes without complications like renal failure and diabetic keto acidosis were studied.

The result showed that most of the patients in our study were males and majority of patients were in the age group of 50-55.Main ocular manifestation in the study was painful proptosis and pre septal cellulitis is the commonest orbital presentation. Patients also presented with cranial nerve palsy and multiple nerve palsy was common. Bilateral ocular involvement was common in the study group but it was asymmetrical.

Maxillary sinus is commonly involved and increased mucosal thickening was the commonest radiological finding in our study group.

Patients who have blood sugar level of 251-300mg/dl and duration of diabetes between 11-15 years are the one who have the clinical evidence of orbital mucormycosis.

All the patients were subjected to similar treatment strategy of systemic anti-fungal therapy followed by appropriate surgical methods irrespective of the stage of presentation. The changes in the subjective symptoms and objective signs after treatment were evaluated, along with the assessment of development of possible complications.

CONCLUSION

- Rhino- Orbital mucormycosis is a rare but fatal filamentous fungal infection of orbit.
- Infection is commonly seen in patients with uncontrolled diabetes.
- Visual loss and ophthalmoplegia is the common ophthalmic manifestation.
- Management includes intensive antifungal therapy followed by appropriate surgery and adjunctive therapy.
- Residual morbidity and high mortality occurs if clinical diagnosis is delayed.

PATIENT 3:

PRE TREATMENT

PHOTOGRAPH

POST TREATMENT

PHOTOGRAPH

PATIENT 30:

PRE SEPTAL CELLULITIS

PATIENT 7:

ORBITAL CELLULITIS

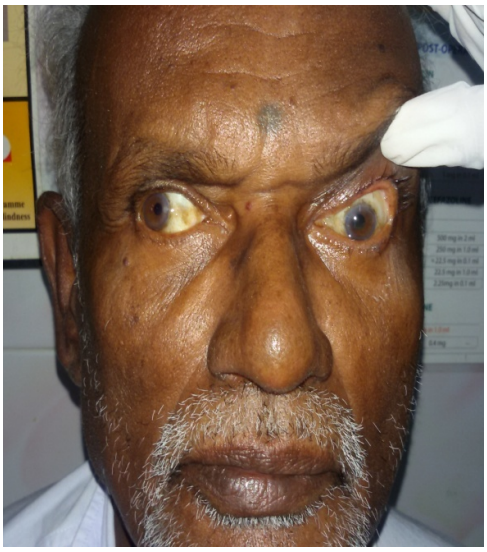
PATIENT 23:

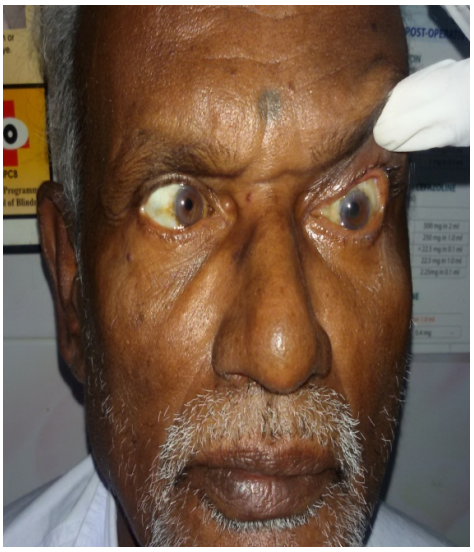
ORBITAL ABSCESS

PATIENT 20:

CAVERNOUS SINUS THROMBOSIS

PATIENT 2:

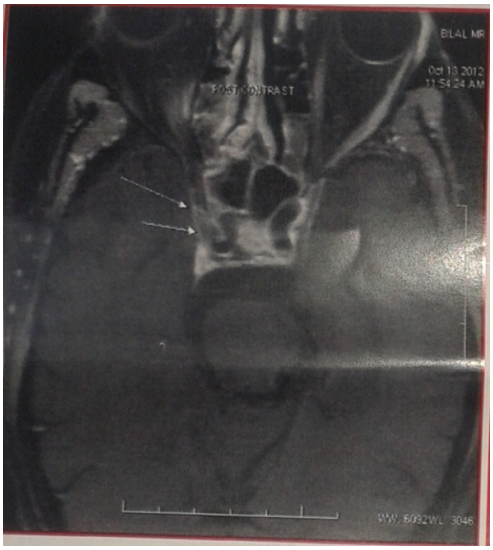




MULTIPLE CRANIAL NERVES WITH MULTIPLE SINUS INVOLVEMENT

PATIENT 14:

SOFT TISSUE THICKENING IN RETRO ORBITAL SPACE WITH INVOLVEMENT OF ORBITAL APEX AND CST



PART III

BIBLIOGRAPHY

TEXT BOOK

1. Anthony J.Bron, Ramesh C.Tripathi and Brenda J. Tripathi and Brenda J.Tripathi Wolff's Anatomy of the Eye and Orbit, 8th edition. The Bony Orbit and Paranasal sinuses ,The ocular appendages.

2. Richard S. Snell, Michael A.Lemp, Clinical Anatomy of the eye, 2nd edition, The orbital cavity.

3. Albert and Jackobiec, Principles and practice of ophthalmology, 2nd edition volume 4,Section13.Lidsand orbit.

4. Sir Sterwart Duke Elder,System of ophthalmology, volume 13,Part 2, The Ocular adenexa.

5. Myron Yanoff, J S Duker,ophthalmology ,section 7 ,Orbit and Oculoplastics,Orbit and Lacrimal gland.

6. Jack Rootman, Disease of Orbit, 2nd edition,Chapter 12 inflammatory diseases.

7. Khalid F Tabbara,Robert A Hyndiuk,Infection of Orbit, first edition.

8. Gilbert Smolin, Khalid Tabbar, John Witcher, Infectious Diseases of the eye.

9. Robert A Zimmerman, Howard Lee, Cranial MRI and CT , 4 th edition chapter 16, The Orbit.

10. Sandra Byrne, Ronald L Green, Ultrasonography of the eye of orbit, 2nd edition.

JOURNALS

1. Shimon Rumelt, Peter A.D.Rubin , Potential sources for Orbital cellulitis, Ocular and adenexal infections.Volume 36,no 3,page 207,Summer 1996, International ophthalmology clinic.

2. Carolyn E Kloek,Peter A.D.Rubin, Role of inflammation in orbital cellulitis ,ocular inflammation ,vol 46, no 2, page 57, Spring 2006, International ophthalmology clinic.

3. Patt B S, Manning S C,Blindness resulting from Orbital complications of sinusitis, vol 104, Otolaryngology Head and neck surgery.

4. N.Suneetha, R R Battu et al, Orbital abscess , Management and outcome volume 48, Issue 2, IJO 2000.

5. Talmi Y P ,Goldschmied-Reouven A, Bakon M Keller N,Barshack I, Wolf M, Horowitz Z,Berkowicz M,Kronberg j. Rhino-orbital-cerebral Mucormycosis.Otolaryngeal Head and neck surgery 2002 ,127:22-31.

6. Yohai RA,Bullock JD,Aziz, Markert RJ.Survival factors in Rhino-orbital-Mucormycosis,1994 ;127 22-31

7. Nithyanandham,S.,M.S.Jacob,R.K.Thomas,M.A.Correa and O.D'Souza, 2003, Rhino-orbito-cerebral mucormycosis.IJO,51;231-236.

PROFORMA

Name	
Age/Sex	
O.P./I.P. No.	
Date	
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Contact No.	
Unit	
Complaints	

OCULAR EXAMINATIONS

SLIT LAMP EXAMINATIONS

RE LE

VISUAL ACTIVITY

LIDS

CONJUNCTIVA

CORNEA

AC

PUPIL

IRIS

LENS

INTRAOCULAR TENSION

EXTRA OCULAR MOVEMENTS

COLOUR VISION

FUNDUS EXAMINATION

DIRECT

INDIRECT

DIPLOPIA CHARTING

HERTELS EXOPHTHALMOMENTRY

B SCAN ULTRASONOGRPHY

LABORATORY INVESTIGATIONS

X-RAY ORBIT/CT SCAN /MRI SCAN

TISSUE BIOPSY / ORITAL FNAC

OTHER DEPARTMENTAL CONSULTATIONS

ENT/ NEUROLOGY/ DIABETOLOGY

FINAL DIAGNOSIS

TREATMENT

MEDICAL/ SURGICAL

FOLLOW UP VISITS

AT THE END OF 1^{ST}, 4^{TH} , 6^{TH} WEEKS AND 3^{RD} , 6^{TH} AND 12^{TH} MONTHS.

ASSESSMENT OF PARAMETERS

VISUAL ACUITY

EXTRA OCULAR MOVEMENTS

SLIT LAMP EXAMINATION

INTRA OCULAR PRESSURE

INDIRECT OPHTHALMOSCOPY

KEY WORDS TO MASTER CHART

1. SN - Serial Number
2. V/A – Visual Acuity
3. SYM – Symptom
4. SPD – Seropurulent Discharge
5. CNP – Cranial Nerve Plasy
6. VD – Visual Deterioration
7. LE – Lid Edema
8. PP – Painful Proptosis
9. CN – Cranial Nerve
10. ORB – Orbital
11. J1 – Preseptal Cellulitis
12. J2 – Orbital Cellulitis
13. J3 – Sub Periosteal Abscess
14. J4 - Orbital Abscess
15. J5- Cavernous Sinus Thrombosis
16. EK – Exposure Keratopathy
17. P – Panophthalmitis
18. ON – Optic Neuropathy
19. M – Maxillary
20. S – Sphenoidal
21. E – Ethmoidal
22. MFL – Multiple Fluid Level
23. MT – Mucosal Thickening
24. BE – Bony Erotion

SN	NAME	AGE	SEX	EYE	VA RE	VA LE	SYM	CN	ORB-MANIFEST	CAUSE OF VD	SINUS	RAD-MANIFEST	FBS	DM (yrs)	DETERIORATION	SYST. ASS
1	Lakshmipathy	51	M	OD	6/9	6/6	SPD	nil	J1	EK	E	MFL	280	8	nil	isolated
2	Veerappan	52	M	OS	6/12	4/60	CNP	M3,4,6	J5	nil	M	MT	309	12	UCD	pulmonary
3	Shanmugam	59	M	OS	6/12	1/60	VD	nil	J4	EK	M	MT	244	7	PC	isolated
4	Narayana samy	51	M	OU	3/60	3/60	PP RE	nil	J1	nil	S	MT	262	14	nil	isolated
5	Paulraj	51	M	OU	6/24	6/36	PP BE	nil	J1	nil	MUL	MT	281	25	nil	isolated
6	mariappan	42	M	OD	6/24	6/9	PP	nil	J1	nil	M	MT	198	11	nil	isolated
7	Sundaram	47	M	OD	6/12	6/6	SPD	nil	J2	nil	M	MT	255	15	nil	isolated
8	Muniyandi	49	M	OD	6/36	6/24	PP	nil	J1	nil	E	MFL	281	13	nil	isolated
9	Padmanabhan	44	M	OU	6/60	6/36	PP BE	nil	J1	nil	MUL	MT	271	9	PC	isolated
10	Pushparaj	57	M	OD	1/2 /60	6/18	VD	nil	J2	EK	M	MT	280	14	nil	isolated
11	Mottaisamy	61	M	OU	4/60	6/12	CNP	sixth	J2	nil	S	MT	314	15	nil	isolated
12	venkatraman	58	M	OS	6/6	6/12	SPD	nil	J1	nil	M	MT	257	6	nil	isolated
13	Chockalingam	52	M	OD	6/12	6/12	SPD	nil	J1	nil	M	BE	277	4	nil	isolated
14	Silal	52	M	OU	3/60	4/60	CNP	M3,4,6	J5	nil	MUL	MT	359	12	nil	GI
15	Velayudham	62	M	OS	5/60	5/60	PP	nil	J1	nil	M	MFL	179	11	nil	isolated
16	Kanaiyan	56	M	OD	PL +	6/12	VD	nil	J2	P	M	MT	298	14	D	disseminated
17	kathirvel	52	M	OS	6/12	6/12	LE	nil	J3	nil	M	MT	265	8	nil	isolated
18	Asaithambi	52	M	OD	6/12	6/12	SPD	nil	J2	nil	M	MT	277	4	nil	isolated
19	Arivazhagan	53	M	OU	HM+	1/2 / 60	VD	nil	J2	CRVO RE	MUL	MT	288	12	nil	isolated
20	Murugan	53	M	OU	3/60	3/60	CNP RE	M 3,4,6	J5	nil	MUL	MT	412	12	UCD	pulmonary
21	Chockalingam	64	M	OU	6/36	6/24	PP BE	nil	J2	nil	MUL	MT	290	8	nil	isolated
22	Chidambaram	56	M	OS	6/9	6/12	SPD	nil	J1	nil	M	MT	255	3	nil	isolated
23	Perumal	53	M	OU	6/60	6/60	PP BE	nil	J1	nil	MUL	MT	152	16	nil	isolated
24	kaniappan	53	M	OU	6/36	6/60	PP BE	nil	J1	nil	MUL	MT	250	6	nil	isolated
25	Pushpavalli	54	F	OD	6/24	6/24	LE	nil	J1	nil	M	BE	168	19	nil	isolated
26	gunabhusham	52	F	OS	6/18	5/60	CNP	third	J1	nil	M	MT	316	13	nil	isolated
27	Ellamal	54	F	OU	3/60	1/60	VD LE	nil	J2	ON	MUL	MT	249	14	nil	isolated
28	Lakshme	54	F	OU	6/24	6/24	PP BE	nil	J1	nil	E	MT	188	12	nil	isolated
29	kanaga	55	F	OD	6/9	6/9	SPD	nil	J1	nil	M	MT	238	20	nil	cutaneous
30	muthuselvi	55	F	OS	6/6	6/9	LE	nil	J1	nil	M	MT	180	6	nil	isolated